

04-724-940.

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OM protein - protein search, using sw model

Run on: July 15, 2004, 17:59:28 ; Search time 54 Seconds  
(without alignments)  
219.759 Million cell updates/sec

Title: US-09-724-940-42  
Perfect score: 217  
Sequence: 1 DAEFRHDSGYEVHHQKLVEFF.....DVGSNKGAIIGLMVGGVVIA 42

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : A\_Geneseq\_29Jan04:\*

- 1: geneseqp1980s:\*
- 2: geneseqp1990s:\*
- 3: geneseqp2000s:\*
- 4: geneseqp2001s:\*
- 5: geneseqp2002s:\*
- 6: geneseqp2003as:\*
- 7: geneseqp2003bs:\*
- 8: geneseqp2004s:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

#### SUMMARIES

Result No.	Score	%		DB	ID	Description
		Query Match	Length			
1	217	100.0	42	2	AAR20330	Aar20330 Sequence
2	217	100.0	42	2	AAR60366	Aar60366 Beta-amyl
3	217	100.0	42	2	AAR95248	Aar95248 Beta/A4-a
4	217	100.0	42	2	AAR94591	Aar94591 Alzheimer
5	217	100.0	42	2	AAW12828	Aaw12828 Beta A4 p
6	217	100.0	42	2	AAW64507	Aaw64507 Neurotoxi
7	217	100.0	42	2	AAW42989	Aaw42989 Full leng
8	217	100.0	42	2	AAW47230	Aaw47230 Beta-amyl
9	217	100.0	42	2	AAW49691	Aay49691 Human bet

10	217	100.0	42	2	AAW99585	Aaw99585	Mutant ag
11	217	100.0	42	2	AAW81474	Aaw81474	Synthetic
12	217	100.0	42	2	AAV08607	Aay08607	Human bet
13	217	100.0	42	2	AAW29093	Aaw29093	A-beta-bi
14	217	100.0	42	2	AAV25137	Aay25137	Human amy
15	217	100.0	42	2	AAW92726	Aaw92726	Human tac
16	217	100.0	42	2	AAV33407	Aay33407	Human amy
17	217	100.0	42	3	AAV96956	Aay96956	Beta-amy1
18	217	100.0	42	4	AAB86134	Aab86134	Human Alz
19	217	100.0	42	4	AAB35589	Aab35589	Beta/A4-a
20	217	100.0	42	4	AAB49098	Aab49098	Human amy
21	217	100.0	42	4	AAB48497	Aab48497	Human amy
22	217	100.0	42	4	AAB91779	Aab91779	Amyloid b
23	217	100.0	42	4	AAB91812	Aab91812	Amyloid b
24	217	100.0	42	4	AAB82622	Aab82622	Amyloid-b
25	217	100.0	42	4	AAB49395	Aab49395	Human amy
26	217	100.0	42	4	AAB48830	Aab48830	Human amy
27	217	100.0	42	4	AAE05484	Aae05484	Human pep
28	217	100.0	42	5	ABB81321	Abb81321	Amyloid p
29	217	100.0	42	5	AAU80961	Aau80961	Human amy
30	217	100.0	42	5	AAU98727	Aau98727	Human amy
31	217	100.0	42	5	ABG94281	Abg94281	Amyloid b
32	217	100.0	42	5	AAE21438	Aae21438	Human bet
33	217	100.0	42	5	ABB76029	Abb76029	Beta amyl
34	217	100.0	42	5	AAE25335	Aae25335	Modified
35	217	100.0	42	5	AAO15848	Aao15848	Beta-amy1
36	217	100.0	42	5	AAU76483	Aau76483	Amino aci
37	217	100.0	42	5	AAE26080	Aae26080	Beta amyl
38	217	100.0	42	5	AAG68314	Aag68314	Human bet
39	217	100.0	42	5	AAU96896	Aau96896	Human Amy
40	217	100.0	42	5	AAU93988	Aau93988	Human bet
41	217	100.0	42	5	AAE26300	Aae26300	Human bet
42	217	100.0	42	5	ABG80593	Abg80593	Human amy
43	217	100.0	42	5	AAM51864	Aam51864	Neuronal
44	217	100.0	42	5	AAU75433	Aau75433	Amyloid p
45	217	100.0	42	5	ABB83306	Abb83306	Amyloid-b

# ALIGNMENTS

## RESULT 1

AAR20330

ID AAR20330 standard; peptide; 42 AA.

XX

AC AAR20330;

XX

DT 25-MAR-2003 (revised)

DT 14-APR-1992 (first entry)

XX

DE Sequence of A99 (beta-amyloid core domain).

XX

KW Transgenic mice; Alzheimer's disease; diagnosis; beta-amaloid precursor;  
KW plaque core protein.

XX

OS Homo sapiens.

XX

PN WO9119810-A.  
 XX  
 PD 26-DEC-1991.  
 XX  
 PF 15-JUN-1990; 90US-00538857.  
 XX  
 PR 15-JUN-1990; 90US-00538857.  
 PR 17-JUN-1991; 91US-00716725.  
 XX  
 PA (CALD ) CALIFORNIA BIOTECHNOLOGY INC.  
 XX  
 PI Cordell B;  
 XX  
 DR WPI; 1992-024426/03.  
 XX  
 PT Transgenic mice as models for studying Alzheimer's disease proteins -  
 PT contg. cells with promoter and beta-amyloid precursor protein  
 PT deoxyribonucleic acid, useful for testing anti-alzheimer's drugs.  
 XX  
 PS Disclosure; Fig 3; 98pp; English.  
 XX  
 CC The inventors specifically claim transgenic mice contg. DNA encoding A42  
 CC (beta-amyloid precursor protein) (AAR20330), A99 (beta-amyloid carboxy  
 CC tail) (AAR20329), A695 (beta-amyloid precursor protein), A751 (precursor  
 CC plus inhibitor) or A4i (protease inhibitor) (AAR20328). Human fibroblast  
 CC cDNA clone lambdaAPCP168i4 was deposited at ATCC on July 1, 1987 and has  
 CC accession No. 40347. The promoter is pref. the NSE promoter with the A751  
 CC or the A695 sequence. (Updated on 25-MAR-2003 to correct PR field.)  
 CC (Updated on 25-MAR-2003 to correct PA field.)  
 XX  
 SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 1.7e-24;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 2  
 AAR60366

ID AAR60366 standard; peptide; 42 AA.  
 XX  
 AC AAR60366;  
 XX  
 DT 25-MAR-2003 (revised)  
 DT 15-MAR-1995 (first entry)  
 XX  
 DE Beta-amyloid (1-42).  
 XX  
 KW Amyloid precursor protein; APP; Alzheimer's disease; beta-amyloid;  
 KW anti-beta-amyloid antibody; diagnosis.  
 XX  
 OS Homo sapiens.  
 XX

PN WO9417197-A1.  
 XX  
 PD 04-AUG-1994.  
 XX  
 PF 24-JAN-1994; 94WO-JP000089.  
 XX  
 PR 25-JAN-1993; 93JP-00010132.  
 PR 05-FEB-1993; 93JP-00019035.  
 PR 16-NOV-1993; 93JP-00286985.  
 PR 28-DEC-1993; 93JP-00334773.  
 XX  
 PA (TAKE ) TAKEDA CHEM IND LTD.  
 XX  
 PI Suzuki N, Odaka A, Kitada C;  
 XX  
 DR WPI; 1994-264110/32.  
 XX  
 PT Antibodies recognising specific parts of beta-amyloid - can be used for  
 PT diagnosis of diseases implicating beta-amyloid, such as Alzheimer's  
 PT disease.  
 XX  
 PS Disclosure; Page 83; 116pp; Japanese.  
 XX  
 CC Antibodies which recognise specific subfragments of the beta-amyloid  
 CC protein are claimed. Specifically, the antibodies (which are pref.  
 CC monoclonal) recognise residues 1-16 and/or 1-28 from the N-terminal  
 CC portion of beta-amyloid or they recognise residues 25-35 or 35-43 from  
 CC the C-terminal portion. The antibodies are useful for assaying beta-  
 CC amyloid and its derivatives for diagnosis of Alzheimer's disease.  
 CC (Updated on 25-MAR-2003 to correct PN field.)  
 XX  
 SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 1.7e-24;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 3  
 AAR95248

ID AAR95248 standard; peptide; 42 AA.  
 XX  
 AC AAR95248;  
 XX  
 DT 20-JAN-1997 (first entry)  
 XX  
 DE Beta/A4-amyloid peptide.  
 XX  
 KW Beta/A4-amyloid peptide; tissue plasminogen activator;  
 KW Alzheimer's disease; stimulation; investigation; pathogenesis;  
 KW hereditary cerebral haemorrhage with amyloidosis-Dutch type; control;  
 KW cerebral amyloid angiopathy; cerebral; haemorrhage; hemorrhage.  
 XX

OS Homo sapiens.  
 XX  
 PN WO9615799-A1.  
 XX  
 PD 30-MAY-1996.  
 XX  
 PF 22-NOV-1995; 95WO-US015007.  
 XX  
 PR 22-NOV-1994; 94US-00347144.  
 XX  
 PA (RUTF ) UNIV RUTGERS STATE NEW JERSEY.  
 XX  
 PI Anderson S;  
 XX  
 DR WPI; 1996-268332/27.  
 XX  
 PT Use of agents which bind beta-amyloid peptide - for diagnosis, prevention  
 PT and treatment of vascular damage caused by amyloid deposits, partic. in  
 PT haemorrhaging and Alzheimer's disease.  
 XX  
 PS Example 1; Fig 1; 52pp; English.  
 XX  
 CC To investigate the effects of beta-amyloid peptide (BAP) on tissue  
 CC plasminogen activator (t-PA) 3 synthetic peptides were used. One peptide  
 CC contained 42 amino acids and corresp. to the full length BAP (AAR95248).  
 CC The other 2 peptides (AAR95249 and 50) contained the 28 N-terminal  
 CC residues of the BAP found in Alzheimer's disease and hereditary cerebral  
 CC haemorrhage with amyloidosis-Dutch type (HCHWA-D), respectively. In an  
 CC assay to determine the effect of the peptides on t-PA activation, each  
 CC peptide (AAR95248, 49 and 50) gave 1st order rate constant of activation  
 CC (k(app)) values of 13.4, 13.9 and 14.5, respectively, compared to 1.7 and  
 CC 7.8 for nill and fibrinogen controls. The results demonstrate that the  
 CC BAP are able to stimulate t-PA activity in vitro, which is significant in  
 CC that it provides a means for investigating and controlling the  
 CC pathogenesis of Alzheimer's disease, HCHWA-D and cerebral amyloid  
 CC angiopathy related cerebral haemorrhage  
 XX  
 SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 1.7e-24;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 4  
 AAR94591  
 ID AAR94591 standard; peptide; 42 AA.  
 XX  
 AC AAR94591;  
 XX  
 DT 25-MAR-2003 (revised)  
 DT 21-AUG-1996 (first entry)  
 XX

DE Alzheimer amyloid beta-protein active site sequence.  
 XX  
 KW Beta-amyloid; Alzheimer's disease; cholinesterase; lipase; ebelactone-A;  
 KW serine protease; para-amidinophenylmethanesulphonyl fluoride; inhibition;  
 KW complex formation; alpha(1)-antichymotrypsin; Down's diseases; ageing.  
 XX  
 OS Synthetic.  
 XX  
 PN US5506097-A.  
 XX  
 PD 09-APR-1996.  
 XX  
 PF 10-JAN-1994; 94US-00179574.  
 XX  
 PR 24-AUG-1990; 90US-00572671.  
 PR 13-JAN-1992; 92US-00819361.  
 PR 13-JAN-1993; 93WO-US000325.  
 XX  
 PA (HARD ) HARVARD COLLEGE.  
 XX  
 PI Kayyali U, Potter H;  
 XX  
 DR WPI; 1996-200270/20.  
 XX  
 PT Inhibiting enzymatic activity of Alzheimer amyloid beta-protein - using p  
 PT -amidino:phenyl:methanesulphonyl fluoride or ebelactone A, for treatment,  
 PT study and diagnosis of Alzheimer's disease, etc.  
 XX  
 PS Disclosure; Fig 1; 17pp; English.  
 XX  
 CC This is the sequence of a fragment of the beta-amyloid protein associated  
 CC with Alzheimer's disease. The protein contains esterase (cholinesterase  
 CC and lipase) activities based on active site similarities with serine  
 CC proteases (see AAR94592-96). The esterase activity of the beta-amyloid  
 CC protein is inhibited by the cpds. of the invention i.e. ebelactone A or  
 CC para-amidinophenylmethanesulphonyl fluoride. Inhibition of these  
 CC activities prevent complex formation between the beta-amyloid protein and  
 CC alpha(1)-antichymotrypsin, thus can be used to treat, study or diagnose  
 CC Alzheimer's or Down's diseases or normal ageing. (Updated on 25-MAR-2003  
 CC to correct PF field.)  
 XX  
 SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 1.7e-24;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 5  
 AAW12828  
 ID AAW12828 standard; peptide; 42 AA.  
 XX  
 AC AAW12828;

XX  
 DT 08-DEC-1997 (first entry)  
 XX  
 DE Beta A4 peptide.  
 XX  
 KW Beta A4 peptide; alzheimer's disease; peptide aggregation; brain;  
 KW therapy; inhibitor.  
 XX  
 OS Homo sapiens.  
 XX  
 PN WO9707403-A1.  
 XX  
 PD 27-FEB-1997.  
 XX  
 PF 23-JUL-1996; 96WO-US012034.  
 XX  
 PR 16-AUG-1995; 95US-00515606.  
 XX  
 PA (HMRI ) HOECHST MARION ROUSSEL INC.  
 XX  
 PI Goyal S, Paul J, Riedel NG, Sahasrabudhe SR;  
 XX  
 DR WPI; 1997-165447/15.  
 XX  
 PT Determn. of the degree of betaA4 peptide aggregation using binding agent  
 PT - used to screen cpds. for possible use in Alzheimer's disease treatment.  
 XX  
 PS Disclosure; Page 10; 18pp; English.  
 XX  
 CC This sequence represents the beta A4 peptide. The degree of aggregation  
 CC of this peptide is determined using the method of the invention. The beta  
 CC A4 peptide is present in the brain of Alzheimer's disease patients, but  
 CC not in the brain of non-Alzheimer's disease individuals. The peptide  
 CC clumps or aggregates in the brain of Alzheimer's disease patients, where  
 CC it may be responsible for the destruction of normal brain cells. Once the  
 CC clumps or aggregates form, the formulation is almost irreversible. The  
 CC method of the invention comprises reacting this sequence with a binding  
 CC reagent capable of binding to it only in its non-aggregated state, to  
 CC form an amount of a beta A4 peptide-bound reagent and an amount of  
 CC protein free reagent. The amount of the beta A4 peptide, binding reagent  
 CC complex is then measured. Compounds which inhibit aggregation of beta A4  
 CC peptide are potentially useful for treatment of Alzheimer's disease  
 XX  
 SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 1.7e-24;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 6  
 AAW64507  
 ID AAW64507 standard; peptide; 42 AA.

XX  
 AC AAW64507;  
 XX  
 DT 20-OCT-1998 (first entry)  
 XX  
 DE Neurotoxic beta-amyloid peptide decoy peptide #20.  
 XX  
 KW Beta-amyloid peptide; beta-AP; neuropeptide; neurotoxin; calcium influx;  
 KW aggregate; Alzheimers disease; decoy; treatment.  
 XX  
 OS Synthetic.  
 XX  
 PN WO9830229-A1.  
 XX  
 PD 16-JUL-1998.  
 XX  
 PF 09-JAN-1998; 98WO-US000653.  
 XX  
 PR 10-JAN-1997; 97US-0035847P.  
 PR 29-OCT-1997; 97US-00960188.  
 XX  
 PA (MASI ) MASSACHUSETTS INST TECHNOLOGY.  
 XX  
 PI Ingram VM, Blanchard BJ;  
 XX  
 DR WPI; 1998-398795/34.  
 XX  
 PT Inhibition of aggregation of, e.g. beta-amyloid peptide - by  
 PT administering decoy peptide or other calcium-influx inhibitor, useful  
 PT for, e.g. treating Alzheimer's disease.  
 XX  
 PS Example 8; Page 46; 68pp; English.  
 XX  
 CC AAW64488-W64517 are decoy peptides that bind to a neurotoxic beta-amyloid  
 CC peptide (beta-AP) and reduces the ability of beta-AP's to form aggregates  
 CC that increase calcium influx into neuronal cells. Such peptides can be  
 CC used in the treatment of diseases associated with neurotoxic aggregates  
 CC of beta-AP specifically Alzheimer's disease. The peptides are  
 CC administered at 0.001-1000 (especially 0.2-20) mg/kg, by injection and  
 CC orally, or from slow-release implants  
 XX  
 SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 1.7e-24;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 7  
 AAW42989  
 ID AAW42989 standard; peptide; 42 AA.  
 XX  
 AC AAW42989;



XX  
 DT 01-MAY-1998 (first entry)  
 XX  
 DE Full length beta-amyloid peptide (BAP).  
 XX  
 KW Beta-amyloid peptide; BAP; extracellular BAP plaque;  
 KW cerebrovascular deposit; Alzheimers disease; Downs syndrome;  
 KW amyloid precursor protein; APP; secretase; BAP aggregation;  
 KW abnormal proteolytic cleavage.  
 XX  
 OS Homo sapiens.  
 XX  
 PN US5703209-A.  
 XX  
 PD 30-DEC-1997.  
 XX  
 PF 05-JUN-1995; 95US-00464248.  
 XX  
 PR 01-MAY-1992; 92US-00877675.  
 PR 20-SEP-1993; 93US-00123659.  
 XX  
 PA (AMCY ) AMERICAN CYANAMID CO.  
 XX  
 PI Jacobsen JS, Vitek MP;  
 XX  
 DR WPI; 1998-076482/07.  
 XX  
 PT Amyloid precursor protein fusion polypeptides - comprising APP fragment  
 PT and marker, useful for research and drug screening.  
 XX  
 PS Disclosure; Col 7; 84pp; English.  
 XX  
 CC The present sequence represents a beta-amyloid peptide (BAP). Abnormal  
 CC accumulation of extracellular BAP in plaques and cerebrovascular deposits  
 CC is characteristic in brains of individuals suffering from Alzheimers  
 CC disease and Downs syndrome. BAP is a poorly soluble, self-aggregating  
 CC protein which is derived from a larger amyloid precursor protein (APP).  
 CC APP is expressed as an integral membrane protein, and is cleaved by  
 CC secretase, between BAP 16Lys and 17Leu. Cleavage at this site precludes  
 CC amyloidogenesis and results in the release of the amino-terminal APP  
 CC fragment. Three major isoforms of APP exist: APP-695, APP-751 and APP-  
 CC 770. These isoforms are derived by alternative splicing. APP-ARP 751 is a  
 CC deletion construct of APP-751, which has a deletion of 276 amino acids to  
 CC within 15 amino acids of the BAP domain. APP can be used as a substrate  
 CC for studying abnormal proteolytic cleavage which results in the release  
 CC of BAP, and also to screen for drugs that will inhibit such cleavage  
 XX  
 SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 1.7e-24;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 8

AAW47230

ID AAW47230 standard; peptide; 42 AA.

XX

AC AAW47230;

XX

DT 22-MAY-1998 (first entry)

XX

DE Beta-amyloid peptide residues 1-42.

XX

KW Screening assay; beta-amyloid peptide; treatment; amyloidosis disease;

KW Alzheimer's disease.

XX

OS Homo sapiens.

XX

PN US5721106-A.

XX

PD 24-FEB-1998.

XX

PF 12-SEP-1994; 94US-00304585.

XX

PR 13-AUG-1991; 91US-00744767.

XX

PA (MINU ) UNIV MINNESOTA.

PA (HARD ) HARVARD COLLEGE.

XX

PI Mantyh PW, Maggio JE;

XX

DR WPI; 1998-168404/15.

XX

PT New in vitro screening assay for Alzheimer's disease drugs - comprises

PT assessing binding of labelled beta-amyloid peptide to silk sample.

XX

PS Claim 8; Col 29-30; 36pp; English.

XX

CC The present sequence was used in the development of a novel in vitro  
 CC screening assay for agents capable of affecting the deposition of beta-  
 CC amyloid peptide (BAP) on tissue. The method comprises contacting a silk  
 CC sample with labelled BAP, optionally in the presence of a test agent,  
 CC detecting the amount of label bound to the silk and assessing the effect  
 CC of the agent on the deposition of BAP. Agents that inhibit binding of BAP  
 CC to silk are potentially useful for treating amyloidosis diseases,  
 CC especially Alzheimer's disease

XX

SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;

Best Local Similarity 100.0%; Pred. No. 1.7e-24;

Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

|||||

Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 9

AA49691

ID AA49691 standard; peptide; 42 AA.

XX

AC AA49691;

XX

DT 13-JAN-2000 (first entry)

XX

DE Human beta amyloid precursor protein peptide.

XX

KW Human; beta amyloid precursor protein; APP; beta secretase inhibition;

KW alpha secretase; neurological disorder; Alzheimer's disease;

KW Downs syndrome; mutation.

XX

OS Homo sapiens.

XX

PN WO9951752-A1.

XX

PD 14-OCT-1999.

XX

PF 31-MAR-1999; 99WO-JP001701.

XX

PR 31-MAR-1998; 98JP-00101821.

XX

PA (CHUS ) CHUGAI SEIYAKU KK.

XX

PI Ozawa K, Ikeda S, Tabira T;

XX

DR WPI; 1999-620208/53.

XX

PT A cell line which produces beta amyloid precursor protein, used in the

PT investigation of neurological disorders such as Alzheimer's disease.

XX

PS Disclosure; Page 41; 70pp; Japanese.

XX

CC The present invention describes a cell line which produces beta amyloid

CC precursor protein (APP) and expresses alpha secretase activity but

CC expresses beta secretase activity only under an external stimulus. Also

CC described is a cloning method for DNA encoding beta secretase,

CC comprising: (1) inserting a DNA library into the cell line, expressing

CC the inserted DNA, and selecting cells expressing beta secretase then

CC isolating the beta secretase DNA from them; or (2) isolating nucleic acid

CC from the cell line with or without external stimulation and performing

CC subtractive cloning to identify DNA expressed only under stimulation.

CC Products from the present invention may be used in the investigation of

CC neurological disorders such as Alzheimer's disease and Downs syndrome and

CC in particular the association of mutations of the beta APP with them. The

CC present sequence represents a human beta APP peptide

XX

SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;

Best Local Similarity 100.0%; Pred. No. 1.7e-24;

Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

|||||

Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 10

AAW99585

ID AAW99585 standard; peptide; 42 AA.

XX

AC AAW99585;

XX

DT 22-JUN-1999 (first entry)

XX

DE Mutant aggregating amyloid-beta peptide.

XX

KW Aggregation; amyloid-beta peptide; fluorescent group; detection;

KW diagnosis; Alzheimer's disease.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO9908695-A1.

XX

PD 25-FEB-1999.

XX

PF 13-AUG-1998; 98WO-US016809.

XX

PR 14-AUG-1997; 97US-0055660P.

XX

PA (REGC ) UNIV CALIFORNIA.

XX

PI Glabe C, Garzon-Rodriguez W;

XX

DR WPI; 1999-190112/16.

XX

PT New fluorescent labeled amyloid A-beta peptides.

XX

PS Example 1; Page 21; 50pp; English.

XX

CC This sequence corresponds to a mutant aggregating amyloid-beta peptide  
 CC which can be covalently labelled with a fluorescent group. The detection  
 CC or monitoring of an amyloid aggregate in a sample can be used to diagnose  
 CC or detect a predisposition to Alzheimer's disease. The screening assays  
 CC can be used to identify compounds for the treatment or amelioration of  
 CC Alzheimer's disease or its symptoms. The fluorescent derivatives of the  
 CC amyloid-beta peptide are also useful for exploring other aspects of  
 CC amyloid structure

XX

SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;

Best Local Similarity 100.0%; Pred. No. 1.7e-24;

Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

|||||

Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 11

AAW81474

ID AAW81474 standard; peptide; 42 AA.

XX

AC AAW81474;

XX

DT 28-JAN-1999 (first entry)

XX

DE Synthetic amyloid beta (Abeta) peptide 9 (residues 1-42).

XX

KW Amyloid beta; Abeta; deoxygenated solvent; evaporative deposition;  
KW research; neurotoxicity; free-radical; glutamine synthetase.

XX

OS Synthetic.

XX

PN US5840838-A.

XX

PD 24-NOV-1998.

XX

PF 29-FEB-1996; 96US-00609090.

XX

PR 29-FEB-1996; 96US-00609090.

XX

PA (KENT ) UNIV KENTUCKY RES FOUND.

XX

PI Aksenov M, Carney JM, Hensley K, Butterfield DA;

XX

DR WPI; 1999-034120/03.

XX

PT Process for treating synthetic amyloid beta peptides - by organic solvent  
PT treatment, useful for studying neurotoxicity.

XX

PS Claim 5; Col 11-12; 14pp; English.

XX

CC Sequences AAW81466 to AAW81476 represent synthetic amyloid beta (Abeta)  
CC peptides. The invention provides a process for treating a synthetic Abeta  
CC peptide that comprises dissolving the peptide in a deoxygenated solvent  
CC selected from trifluoroethanol, hexafluorocyclohexane, dimethyl  
CC sulphoxide, morpholinopropanesulphonic acid, dimethylformamide and  
CC acetonitrile to a concentration of 0.01-10 mg/ml, incubating the solution  
CC at 20-65 deg. C for 0.5-4 hour, and removing the solvent by "evaporative  
CC deposition" in 5-10 minutes. Synthetic amyloid beta peptides are useful  
CC as research tools for studying neurotoxicity resulting from Abeta peptide  
CC -enhanced free-radical production. The treatment increases the activity  
CC of the synthetic Abeta peptides in tests to determine free-radical  
CC generating capacity and glutamine synthetase inactivation

XX

SQ Sequence 42 AA;

Query Match 100.0%; Score 217; DB 2; Length 42;

Best Local Similarity 100.0%; Pred. No. 1.7e-24;

Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

|||||

Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 12

AAY08607

ID AAY08607 standard; protein; 42 AA.

XX

AC AAY08607;

XX

DT 05-AUG-1999 (first entry)

XX

DE Human beta-amyloid precursor core protein A42.

XX

KW APP; beta-amyloid precursor protein; human; transgenic mice; pathology;

KW Alzheimer's disease; model; therapeutic compound; brain; mechanism;

KW nerve tissue specific promoter; synthesis; inhibitor; deposition;

KW plaque formation; treatment; A42.

XX

OS Homo sapiens.

XX

PN US5912410-A.

XX

PD 15-JUN-1999.

XX

PF 13-APR-1995; 95US-00422333.

XX

PR 15-JUN-1990; 90US-00538857.

PR 17-JUN-1991; 91US-00716725.

PR 21-OCT-1994; 94US-00327381.

XX

PA (SCIO-) SCIOS INC.

XX

PI Cordell B;

XX

DR WPI; 1999-357231/30.

XX

PT Transgenic mice useful for studying compounds potentially useful in the  
PT treatment of Alzheimer's disease.

XX

PS Disclosure; Fig 3; 72pp; English.

XX

CC This invention describes novel transgenic mice expressing proteins  
CC related to the pathology of Alzheimer's disease and which provide models  
CC for studying potentially therapeutic compounds. The transgenic mice  
CC contain a DNA sequence encoding a beta-amyloid precursor protein (APP)  
CC and a nerve tissue specific promoter operably linked to the beta-APP  
CC allowing its expression to form beta-amyloid protein deposits in the  
CC animal's brain. The transgenic mouse is useful for elucidating the  
CC molecular mechanisms involved in the synthesis of and, more importantly,  
CC inhibiting the synthesis and deposition of beta-amyloid proteins (most  
CC importantly in the brain where plaque formation is associated with  
CC Alzheimer's disease) by inhibiting production and/or increasing cleavage  
CC after production. The transgenic animals provide useful models for  
CC studying the in vivo relationships of the proteins to each other and to  
CC other compounds being tested for their usefulness in treating Alzheimer's  
CC disease

XX

SQ Sequence 42 AA;

Query Match

100.0%; Score 217; DB 2; Length 42;

Best Local Similarity 100.0%; Pred. No. 1.7e-24;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
|||||  
Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 13

AAW29093

ID AAW29093 standard; peptide; 42 AA.

XX

AC AAW29093;

XX

DT 20-JUL-1999 (first entry)

XX

DE A-beta-binding peptide 1-42.

XX

KW Cyclosporin; A-beta peptide; conjugate; neurological disease; Alzheimer;

KW multiple sclerosis; amyotrophic lateral sclerosis; ALS;

KW non-immunosuppressive; amyloid plaque formation.

XX

OS Homo sapiens.

XX

PN WO9910374-A1.

XX

PD 04-MAR-1999.

XX

PF 25-AUG-1998; 98WO-US017544.

XX

PR 26-AUG-1997; 97US-0057751P.

XX

PA (WISC ) WISCONSIN ALUMNI RES FOUND.

XX

PI Rich DH, Solomon ME;

XX

DR WPI; 1999-276928/23.

XX

PT New A $\beta$ -binding peptide conjugates and CsA analogs - useful in treatment  
PT of neurological diseases e.g. Alzheimer's disease, Multiple Sclerosis  
PT etc.

XX

PS Claim 5; Page 98; 129pp; English.

XX

New conjugates are disclosed which are of formula A-Z, in which: A is (1) a cyclosporin A analogue described in AAW29087 or (2) an FK506 binding peptide inhibitor; and Z is a polypeptide comprising 5 or more contiguous residues of A-beta peptide. The compounds are novel chemical inducers of dimerization which are non-immunosuppressive and which are inhibitors of A-beta peptide aggregation and deposition in amyloid plaques. The adverse consequences of amyloid plaque formation can be prevented or ameliorated by sequestering the A-beta peptide in monomeric form with a conjugate which links the A-beta to cyclophilin or FKBP, therefore providing a mechanism to minimize the amount of free A-beta available for fibril formation and deposition. The compounds can be used for the treatment of Alzheimer's disease, multiple sclerosis and amyotrophic lateral sclerosis









OM protein - protein search, using sw model

Run on: July 15, 2004, 18:03:59 ; Search time 18 Seconds  
(without alignments)  
120.461 Million cell updates/sec

Title: US-09-724-940-42  
Perfect score: 217  
Sequence: 1 DAEFRHDSGYEVHHQKLVFF.....DVGSNKGAIIGLMVGGVVIA 42

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 389414 seqs, 51625971 residues

Total number of hits satisfying chosen parameters: 389414

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : Issued\_Patents\_AA:\*  
1: /cgn2\_6/ptodata/2/iaa/5A\_COMB.pep:\*  
2: /cgn2\_6/ptodata/2/iaa/5B\_COMB.pep:\*  
3: /cgn2\_6/ptodata/2/iaa/6A\_COMB.pep:\*  
4: /cgn2\_6/ptodata/2/iaa/6B\_COMB.pep:\*  
5: /cgn2\_6/ptodata/2/iaa/PCTUS\_COMB.pep:\*  
6: /cgn2\_6/ptodata/2/iaa/backfiles1.pep:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

#### SUMMARIES

Result No.	Score	% Query		Length	DB	ID	Description
		Match					
1	217	100.0		42	1	US-07-744-767A-2	Sequence 2, Appli
2	217	100.0		42	1	US-08-179-574-1	Sequence 1, Appli
3	217	100.0		42	1	US-08-347-144-1	Sequence 1, Appli
4	217	100.0		42	1	US-08-462-859A-19	Sequence 19, Appl
5	217	100.0		42	1	US-08-123-659A-19	Sequence 19, Appl
6	217	100.0		42	1	US-08-464-247A-19	Sequence 19, Appl
7	217	100.0		42	1	US-08-464-248A-19	Sequence 19, Appl
8	217	100.0		42	1	US-08-476-464A-1	Sequence 1, Appli
9	217	100.0		42	1	US-08-304-585-2	Sequence 2, Appli
10	217	100.0		42	1	US-08-302-808-5	Sequence 5, Appli
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12	217	100.0	42	2	US-08-433-734-2	Sequence 2, Appli
13	217	100.0	42	2	US-08-609-090-9	Sequence 9, Appli
14	217	100.0	42	2	US-07-737-371E-72	Sequence 72, Appl
15	217	100.0	42	2	US-08-422-333-4	Sequence 4, Appli
16	217	100.0	42	2	US-08-682-245A-4	Sequence 4, Appli
17	217	100.0	42	2	US-08-986-948-5	Sequence 5, Appli
18	217	100.0	42	3	US-08-717-551A-2	Sequence 2, Appli
19	217	100.0	42	3	US-09-388-890-1	Sequence 1, Appli
20	217	100.0	42	3	US-09-005-215-20	Sequence 20, Appl
21	217	100.0	42	4	US-09-242-724-23	Sequence 23, Appl
22	217	100.0	42	4	US-08-922-930-2	Sequence 2, Appli
23	217	100.0	42	4	US-09-660-954-1	Sequence 1, Appli
24	217	100.0	42	4	US-08-923-055-2	Sequence 2, Appli
25	217	100.0	42	4	US-08-922-889-2	Sequence 2, Appli
26	217	100.0	42	4	US-09-731-460-1	Sequence 1, Appli
27	217	100.0	42	4	US-09-133-866-2	Sequence 2, Appli
28	217	100.0	42	5	PCT-US92-06700-2	Sequence 2, Appli
29	217	100.0	42	5	PCT-US93-00325-1	Sequence 1, Appli
30	217	100.0	43	1	US-08-235-400-1	Sequence 1, Appli
31	217	100.0	43	1	US-08-437-067-1	Sequence 1, Appli
32	217	100.0	43	1	US-08-302-808-6	Sequence 6, Appli
33	217	100.0	43	1	US-08-079-511-1	Sequence 1, Appli
34	217	100.0	43	1	US-08-467-607-1	Sequence 1, Appli
35	217	100.0	43	2	US-08-404-831-1	Sequence 1, Appli
36	217	100.0	43	2	US-08-602-264A-3	Sequence 3, Appli
37	217	100.0	43	2	US-08-469-362-1	Sequence 1, Appli
38	217	100.0	43	2	US-08-612-785B-1	Sequence 1, Appli
39	217	100.0	43	2	US-08-475-579A-1	Sequence 1, Appli
40	217	100.0	43	2	US-08-850-392-1	Sequence 1, Appli
41	217	100.0	43	2	US-07-737-371E-70	Sequence 70, Appl
42	217	100.0	43	2	US-08-986-948-6	Sequence 6, Appli
43	217	100.0	43	2	US-08-975-977-1	Sequence 1, Appli
44	217	100.0	43	2	US-08-817-423-1	Sequence 1, Appli
45	217	100.0	43	2	US-08-920-162A-1	Sequence 1, Appli

#### ALIGNMENTS

#### RESULT 1

US-07-744-767A-2

; Sequence 2, Application US/07744767A

; Patent No. 5434050

#### ; GENERAL INFORMATION:

; APPLICANT: Maggio, John E.

; APPLICANT: Mantyh, Patrick W.

; TITLE OF INVENTION: Labelled -Amyloid Peptide and Methods

; TITLE OF INVENTION: for Use in Detecting Alzheimer's Disease

; NUMBER OF SEQUENCES: 3

#### ; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Schwegman, Lundberg & Woessner, P.A.

; STREET: 3500 IDS Center

; CITY: Minneapolis

; STATE: MN

; COUNTRY: USA

; ZIP: 55402

; COMPUTER READABLE FORM:

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; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/07/744,767A
; FILING DATE: 13-AUG-1991
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Muetting, Ann M.
; REGISTRATION NUMBER: 33,977
; REFERENCE/DOCKET NUMBER: 600.226-US-01
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 612-339-0331
; TELEFAX: 612-339-3061
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 42 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: peptide
US-07-744-767A-2

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Query Match          100.0%; Score 217; DB 1; Length 42;
Best Local Similarity 100.0%; Pred. No. 6.3e-26;
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
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Db      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

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# RESULT 2

US-08-179-574-1

```

; Sequence 1, Application US/08179574
; Patent No. 5506097
; GENERAL INFORMATION:
; APPLICANT: Huntington Potter
; APPLICANT: Usamah Kayyali
; TITLE OF INVENTION: Compounds and Methods for Inhibiting
; NUMBER OF SEQUENCES: 6
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Hamilton, Brook, Smith & Reynolds, P.C.
; STREET: Two Militia Drive
; CITY: Lexington
; STATE: Massachusetts
; COUNTRY: U.S.A.
; ZIP: 02173
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/179,574
; FILING DATE:
; CLASSIFICATION: 514

```

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; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 07/819,361
; FILING DATE: 13-JAN-1992
; ATTORNEY/AGENT INFORMATION:
; NAME: Granahan, Patricia
; REGISTRATION NUMBER: 32,227
; REFERENCE/DOCKET NUMBER: HU90-03A3
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 617-861-6240
; TELEFAX: 617-861-9540
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 42 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
US-08-179-574-1

```

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Query Match          100.0%; Score 217; DB 1; Length 42;
Best Local Similarity 100.0%; Pred. No. 6.3e-26;
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
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Db      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

```

# RESULT 3

US-08-347-144-1

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; Sequence 1, Application US/08347144
; Patent No. 5589154
; GENERAL INFORMATION:
; APPLICANT: ANDERSON, STEPHEN
; TITLE OF INVENTION: METHODS FOR THE PREVENTION AND TREATMENT
; TITLE OF INVENTION: OF VASCULAR HEMORRHAGING AND ALZHEIMER'S DISEASE
; NUMBER OF SEQUENCES: 1
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: HOWREY & SIMON
; STREET: 1299 PENNSYLVANIA AVENUE, N.W.
; CITY: WASHINGTON
; STATE: D.C.
; COUNTRY: US
; ZIP: 20004
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/347,144
; FILING DATE:
; CLASSIFICATION: 514
; ATTORNEY/AGENT INFORMATION:
; NAME: AUERBACH, JEFFREY I.
; REGISTRATION NUMBER: 32,680
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (202) 383-7451
; TELEFAX: (202) 383-6610

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; SEQUENCE CHARACTERISTICS:  
; LENGTH: 42 amino acids  
; TYPE: amino acid  
; STRANDEDNESS:  
; TOPOLOGY: linear  
; MOLECULE TYPE: protein  
US-08-462-859A-19

Query Match 100.0%; Score 217; DB 1; Length 42;  
Best Local Similarity 100.0%; Pred. No. 6.3e-26;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
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Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 5

US-08-123-659A-19

; Sequence 19, Application US/08123659A  
; Patent No. 5656477

; GENERAL INFORMATION:

; APPLICANT: Jacobsen, J. S.  
; APPLICANT: Vitek, M. P.  
; TITLE OF INVENTION: No. 5656477e1 Amyloid Precursor and Method of  
; TITLE OF INVENTION: Using Same to Access Agents Which Down-Regulate  
Formation

; TITLE OF INVENTION: of B-Amyloid Peptide

; NUMBER OF SEQUENCES: 19

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Anne Rosenblum  
; STREET: 163 Delaware Avenue, Suite 212  
; CITY: Delmar  
; STATE: New York  
; COUNTRY: U.S.A.  
; ZIP: 12054

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy disk  
; COMPUTER: IBM PC compatible  
; OPERATING SYSTEM: PC-DOS/MS-DOS  
; SOFTWARE: PatentIn Release #1.0, Version #1.25

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/123,659A  
; FILING DATE: 20-SEP-1993  
; CLASSIFICATION: 435

; ATTORNEY/AGENT INFORMATION:

; NAME: Rosenblum, Anne M.  
; REGISTRATION NUMBER: 30,419  
; REFERENCE/DOCKET NUMBER: 31,844-01

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: (518)475-0611  
; TELEFAX: (518)475-0619

; INFORMATION FOR SEQ ID NO: 19:

; SEQUENCE CHARACTERISTICS:  
; LENGTH: 42 amino acids  
; TYPE: amino acid  
; TOPOLOGY: linear



; MOLECULE TYPE: protein  
US-08-123-659A-19

Query Match 100.0%; Score 217; DB 1; Length 42;  
Best Local Similarity 100.0%; Pred. No. 6.3e-26;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
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Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 6

US-08-464-247A-19

; Sequence 19, Application US/08464247A

; Patent No. 5693478

; GENERAL INFORMATION:

; APPLICANT: Jacobsen, J. S.

; APPLICANT: Vitek, M. P.

; TITLE OF INVENTION: No. 5693478el Amyloid Precursor and Method of

; TITLE OF INVENTION: Using Same to Access Agents Which Down-Regulate  
Formation

; TITLE OF INVENTION: of B-Amyloid Peptide

; NUMBER OF SEQUENCES: 19

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: American Cyanamid Company

; STREET: One Campus Drive

; CITY: Parsippany

; STATE: New Jersey

; COUNTRY: United States

; ZIP: 07054

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; SOFTWARE: PatentIn Release #1.0, Version #1.30

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/464,247A

; FILING DATE: 05-JUN-1995

; CLASSIFICATION: 435

; ATTORNEY/AGENT INFORMATION:

; NAME: Barnhard, Elizabeth M.

; REGISTRATION NUMBER: 31,088

; REFERENCE/DOCKET NUMBER: 31,844-03

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: 201-683-2158

; TELEFAX: 201-683-4117

; INFORMATION FOR SEQ ID NO: 19:

; SEQUENCE CHARACTERISTICS:

; LENGTH: 42 amino acids

; TYPE: amino acid

; STRANDEDNESS:

; TOPOLOGY: linear

; MOLECULE TYPE: protein

US-08-464-247A-19

Query Match 100.0%; Score 217; DB 1; Length 42;

Best Local Similarity 100.0%; Pred. No. 6.3e-26;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
|||||  
Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 7

US-08-464-248A-19

; Sequence 19, Application US/08464248A

; Patent No. 5703209

; GENERAL INFORMATION:

; APPLICANT: Jacobsen, J. S.

; APPLICANT: Vitek, M. P.

; TITLE OF INVENTION: No. 5703209el Amyloid Precursor and Method of

; TITLE OF INVENTION: Using Same to Access Agents Which Down-Regulate  
Formation

; TITLE OF INVENTION: of B-Amyloid Peptide

; NUMBER OF SEQUENCES: 19

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: American Cyanamid Company

; STREET: One Cyanamid Plaza

; CITY: Wayne

; STATE: New Jersey

; COUNTRY: United States

; ZIP: 07470-8426

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; SOFTWARE: PatentIn Release #1.0, Version #1.30

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/464,248A

; FILING DATE: 05-JUN-1995

; CLASSIFICATION: 435

; ATTORNEY/AGENT INFORMATION:

; NAME: Barnhard, Elizabeth M.

; REGISTRATION NUMBER: 31,088

; REFERENCE/DOCKET NUMBER: 31,844-02

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: (201)831-3246

; TELEFAX: (201)831-3305

; INFORMATION FOR SEQ ID NO: 19:

; SEQUENCE CHARACTERISTICS:

; LENGTH: 42 amino acids

; TYPE: amino acid

; STRANDEDNESS:

; TOPOLOGY: linear

; MOLECULE TYPE: protein

US-08-464-248A-19

Query Match 100.0%; Score 217; DB 1; Length 42;

Best Local Similarity 100.0%; Pred. No. 6.3e-26;

Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 8

US-08-476-464A-1

; Sequence 1, Application US/08476464A

; Patent No. 5707821

; GENERAL INFORMATION:

; APPLICANT: RYDEL, RUSSELL E.

; APPLICANT: DAPPEN, MICHAEL S.

; TITLE OF INVENTION: THERAPEUTIC INHIBITION OF PHOSPHOLIPASE

; TITLE OF INVENTION: A2 IN A-BETA PEPTIDE-MEDIATED NEURODEGENERATIVE DISEASE

; NUMBER OF SEQUENCES: 2

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: TOWNSEND & TOWNSEND & CREW LLP

; STREET: TWO EMBARCADERO CENTER, 8TH FLOOR

; CITY: SAN FRANCISCO

; STATE: CALIFORNIA

; COUNTRY: U.S.A.

; ZIP: 94111-3834

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; SOFTWARE: PatentIn Release #1.0, Version #1.30

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/476,464A

; FILING DATE: 07-JUN-1995

; CLASSIFICATION: 514

; ATTORNEY/AGENT INFORMATION:

; NAME: STORELLA, JOHN R.

; REGISTRATION NUMBER: 32,944

; REFERENCE/DOCKET NUMBER: 15270-002300

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: (415)326-2400

; TELEFAX: (415)576-0300

; INFORMATION FOR SEQ ID NO: 1:

; SEQUENCE CHARACTERISTICS:

; LENGTH: 42 amino acids

; TYPE: amino acid

; STRANDEDNESS:

; TOPOLOGY: linear

; MOLECULE TYPE: peptide

US-08-476-464A-1

Query Match 100.0%; Score 217; DB 1; Length 42;

Best Local Similarity 100.0%; Pred. No. 6.3e-26;

Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

|||||

Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 9



```

; APPLICANT: KITADA, Chieko
; TITLE OF INVENTION: ANTIBODIES TO B-AMYLOIDS OR THEIR
; TITLE OF INVENTION: DERIVATIVES AND USE THEREOF
; NUMBER OF SEQUENCES: 14
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: DIKE, BRONSTEIN, ROBERTS & CUSHMAN
; STREET: 130 WATER STREET
; CITY: BOSTON
; STATE: MA
; COUNTRY: USA
; ZIP: 02019
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Diskette
; COMPUTER: IBM Compatible
; OPERATING SYSTEM: DOS
; SOFTWARE: FastSEQ Version 1.5
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/302,808
; FILING DATE: 15-SEP-1994
; CLASSIFICATION: 435
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: PCT/JP94/00089
; FILING DATE: 24-JAN-1994
; APPLICATION NUMBER: 010132/1993
; FILING DATE: 25-JAN-1993
; APPLICATION NUMBER: 019035/1993
; FILING DATE: 05-FEB-1993
; APPLICATION NUMBER: 286985/1993
; FILING DATE: 16-NOV-1993
; APPLICATION NUMBER: 334773/1993
; FILING DATE: 28-DEC-1993
; ATTORNEY/AGENT INFORMATION:
; NAME: DAVID, RESNICK S
; REGISTRATION NUMBER: 34,235
; REFERENCE/DOCKET NUMBER: 44631
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 617-523-3400
; TELEFAX: 617-523-6440
; TELEX: 200291 STRE
; INFORMATION FOR SEQ ID NO: 5:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 42 amino acids
; TYPE: amino acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: peptide
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; FRAGMENT TYPE: N-terminal
; ORIGINAL SOURCE:
US-08-302-808-5

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Query Match          100.0%; Score 217; DB 1; Length 42;
Best Local Similarity 100.0%; Pred. No. 6.3e-26;
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

```

Db                    |||||||||||||||||||||||||||||||||||  
1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 11

US-08-268-348A-1

; Sequence 1, Application US/08268348A

; Patent No. 5750374

; GENERAL INFORMATION:

; APPLICANT: Dobeli, Heinz

; APPLICANT: Draeger, Nicholas

; APPLICANT: Trottman, Gerda H

; APPLICANT: Jakob, Peter

; APPLICANT: Stuber, Dietrich

; TITLE OF INVENTION: Process for Producing Hydrophobic

; TITLE OF INVENTION: Polypeptides and Proteins, and Fusion Proteins for Use

in

; TITLE OF INVENTION: Producing Same

; NUMBER OF SEQUENCES: 12

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Hoffmann-La Roche Inc.

; STREET: 340 Kingsland Street

; CITY: Nutley

; STATE: New Jersey

; COUNTRY: U.S.A.

; ZIP: 07110

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; SOFTWARE: PatentIn Release #1.0, Version #1.25

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/268,348A

; FILING DATE: 29-JUN-1994

; CLASSIFICATION: 435

; PRIOR APPLICATION DATA:

; APPLICATION NUMBER: EP 93110755.1

; FILING DATE: 06-JUL-1993

; ATTORNEY/AGENT INFORMATION:

; NAME: Parise, John P.

; REGISTRATION NUMBER: 34,403

; REFERENCE/DOCKET NUMBER: 4105/157

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: (201) 235-6326

; TELEFAX: (201) 235-3500

; INFORMATION FOR SEQ ID NO: 1:

; SEQUENCE CHARACTERISTICS:

; LENGTH: 42 amino acids

; TYPE: amino acid

; TOPOLOGY: linear

; MOLECULE TYPE: peptide

; FRAGMENT TYPE: N-terminal

US-08-268-348A-1

Query Match                    100.0%;   Score 217;   DB 1;   Length 42;

Best Local Similarity       100.0%;   Pred. No. 6.3e-26;

Matches    42;   Conservative       0;   Mismatches       0;   Indels       0;   Gaps       0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 12

US-08-433-734-2

; Sequence 2, Application US/08433734  
 ; Patent No. 5837473  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Maggio, John E.  
 ; APPLICANT: Mantyh, Patrick W.  
 ; TITLE OF INVENTION: Labelled -Amyloid Peptide and Methods  
 ; TITLE OF INVENTION: for Use in Detecting Alzheimer's Disease  
 ; NUMBER OF SEQUENCES: 3  
 ; CORRESPONDENCE ADDRESS:  
 ; ADDRESSEE: Mueting, Raasch, Gebhardt & Schwappach, P.A.  
 ; STREET: P.O. Box 581415  
 ; CITY: Minneapolis  
 ; STATE: MN  
 ; COUNTRY: USA  
 ; ZIP: 55458-1415  
 ; COMPUTER READABLE FORM:  
 ; MEDIUM TYPE: Floppy disk  
 ; COMPUTER: IBM PC compatible  
 ; OPERATING SYSTEM: PC-DOS/MS-DOS  
 ; SOFTWARE: PatentIn Release #1.0, Version #1.25  
 ; CURRENT APPLICATION DATA:  
 ; APPLICATION NUMBER: US/08/433,734  
 ; FILING DATE: 03-MAY-1995  
 ; CLASSIFICATION: 435  
 ; ATTORNEY/AGENT INFORMATION:  
 ; NAME: Mueting, Ann M.  
 ; REGISTRATION NUMBER: 33,977  
 ; REFERENCE/DOCKET NUMBER: 110.00010102  
 ; TELECOMMUNICATION INFORMATION:  
 ; TELEPHONE: 612-305-1220  
 ; TELEFAX: 612-305-1228  
 ; INFORMATION FOR SEQ ID NO: 2:  
 ; SEQUENCE CHARACTERISTICS:  
 ; LENGTH: 42 amino acids  
 ; TYPE: amino acid  
 ; TOPOLOGY: linear  
 ; MOLECULE TYPE: peptide

US-08-433-734-2

Query Match 100.0%; Score 217; DB 2; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 6.3e-26;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 13





```

;  APPLICANT:  Yankner, Bruce A.
;  TITLE OF INVENTION:  SCREENING METHODS TO IDENTIFY
;  TITLE OF INVENTION:  NEUROTOXIN INHIBITORS (AS AMENDED)
;  NUMBER OF SEQUENCES:  77
;  CORRESPONDENCE ADDRESS:
;    ADDRESSEE:  Fish & Richardson, P.C.
;    STREET:  225 Franklin Street
;    CITY:  Boston
;    STATE:  MA
;    COUNTRY:  US
;    ZIP:  02110-2804
;  COMPUTER READABLE FORM:
;    MEDIUM TYPE:  Diskette
;    COMPUTER:  IBM Compatible
;    OPERATING SYSTEM:  Windows95
;    SOFTWARE:  FastSEQ for Windows Version 2.0
;  CURRENT APPLICATION DATA:
;    APPLICATION NUMBER:  US/07/737,371E
;    FILING DATE:  29-JUL-1991
;    CLASSIFICATION:  536
;  PRIOR APPLICATION DATA:
;    APPLICATION NUMBER:  07/559,172
;    FILING DATE:  27-JUL-1990
;  ATTORNEY/AGENT INFORMATION:
;    NAME:  Freeman, John W.
;    REGISTRATION NUMBER:  29,066
;    REFERENCE/DOCKET NUMBER:  00108/028002
;  TELECOMMUNICATION INFORMATION:
;    TELEPHONE:  617-542-5070
;    TELEFAX:  617-542-8906
;    TELEX:  200154
;  INFORMATION FOR SEQ ID NO:  72:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  42 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-07-737-371E-72

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Query Match          100.0%;  Score 217;  DB 2;  Length 42;
Best Local Similarity 100.0%;  Pred. No. 6.3e-26;
Matches  42;  Conservative  0;  Mismatches  0;  Indels  0;  Gaps  0;

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Qy      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
        |||
Db      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

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RESULT 15

US-08-422-333-4

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; Sequence 4, Application US/08422333
; Patent No. 5912410
; GENERAL INFORMATION:
;  APPLICANT:  CORDELL, Barbara L.
;  TITLE OF INVENTION:  TRANSGENIC NON-HUMAN MAMMAL DISPLAYING
;  TITLE OF INVENTION:  THE AMYLOID-FORMING PATHOLOGY OF ALZHEIMER'S DISEASE
;  NUMBER OF SEQUENCES:  30

```

```

;   CORRESPONDENCE ADDRESS:
;   ADDRESSEE:  Scios, Inc.
;   STREET:  2450 Bayshore Parkway
;   CITY:  Mountain View
;   STATE:  CA
;   COUNTRY:  USA
;   ZIP:  94043
;   COMPUTER READABLE FORM:
;   MEDIUM TYPE:  Floppy disk
;   COMPUTER:  IBM PC compatible
;   OPERATING SYSTEM:  PC-DOS/MS-DOS
;   SOFTWARE:  PatentIn Release #1.0, Version #1.30
;   CURRENT APPLICATION DATA:
;   APPLICATION NUMBER:  US/08/422,333
;   FILING DATE:  13-APR-1995
;   CLASSIFICATION:  800
;   ATTORNEY/AGENT INFORMATION:
;   NAME:  Shearer, Peter R.
;   REGISTRATION NUMBER:  28,117
;   REFERENCE/DOCKET NUMBER:  21900-28048.00
;   TELECOMMUNICATION INFORMATION:
;   TELEPHONE:  (415) 966-1550
;   TELEFAX:  (415) 968-2438
;   INFORMATION FOR SEQ ID NO:  4:
;   SEQUENCE CHARACTERISTICS:
;   LENGTH:  42 amino acids
;   TYPE:  amino acid
;   STRANDEDNESS:  single
;   TOPOLOGY:  linear
US-08-422-333-4

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Query Match          100.0%;  Score 217;  DB 2;  Length 42;
Best Local Similarity 100.0%;  Pred. No. 6.3e-26;
Matches   42;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

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```

Qy      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
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Db      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

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Search completed: July 15, 2004, 18:08:49
Job time : 19 secs

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GenCore version 5.1.6  
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 15, 2004, 18:01:09 ; Search time 16 Seconds  
(without alignments)  
252.503 Million cell updates/sec

Title: US-09-724-940-42  
Perfect score: 217  
Sequence: 1 DAEFRHDSGYEVHHQKLVFF.....DVGSNKGAIIGLMVGGVVIA 42

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 283366 seqs, 96191526 residues

Total number of hits satisfying chosen parameters: 283366

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : PIR\_78:\*  
1: pir1:\*  
2: pir2:\*  
3: pir3:\*  
4: pir4:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query		DB	ID	Description
		Match	Length			
1	217	100.0	42	2	PN0512	beta-amyloid prote
2	217	100.0	57	2	E60045	Alzheimer's diseas
3	217	100.0	57	2	F60045	Alzheimer's diseas
4	217	100.0	57	2	G60045	Alzheimer's diseas
5	217	100.0	57	2	D60045	Alzheimer's diseas
6	217	100.0	57	2	A60045	Alzheimer's diseas
7	217	100.0	57	2	B60045	Alzheimer's diseas
8	217	100.0	82	2	PQ0438	Alzheimer's diseas
9	217	100.0	695	1	A49795	Alzheimer's diseas
10	217	100.0	770	1	QRHUA4	Alzheimer's diseas
11	198	91.2	695	2	A27485	Alzheimer's diseas
12	198	91.2	695	2	S00550	Alzheimer's diseas
13	198	91.2	747	2	JH0773	Alzheimer's diseas

14	133	61.3	33	2	S23094	beta-amyloid prote
15	63	29.0	755	2	AI3228	tryptophan 2-monoo
16	62	28.6	755	1	QQAG4T	tryptophan 2-monoo
17	61	28.1	755	1	DAAGWT	tryptophan 2-monoo
18	57	26.3	327	2	S11435	genome polyprotein
19	57	26.3	503	2	S73843	general amino acid
20	56.5	26.0	378	2	S61992	SLG1 protein - yea
21	55.5	25.6	297	2	G69525	formylmethanofuran
22	55.5	25.6	678	2	G71526	3-methyl-2-oxobuta
23	55	25.3	291	2	F95015	glycosyl transfera
24	55	25.3	317	2	H97888	glycosyl transfera
25	55	25.3	488	2	S27652	probable aldehyde
26	55	25.3	3063	2	JS0166	genome polyprotein
27	54.5	25.1	678	2	C81683	3-methyl-2-oxobuta
28	54.5	25.1	832	2	H84848	phospholipase D [i
29	54	24.9	77	2	C97027	feoA-like protein,
30	54	24.9	284	2	S04723	genome polyprotein
31	54	24.9	763	2	AI3443	Na+/H+ antiporter
32	53.5	24.7	708	2	T24727	hypothetical prote
33	53.5	24.7	971	2	D70128	conserved hypothet
34	53	24.4	256	2	G96774	hypothetical prote
35	53	24.4	390	2	C75103	na+/h+ antiporter
36	53	24.4	422	2	D72302	hypothetical prote
37	53	24.4	601	2	T02581	nodulin-like prote
38	53	24.4	1555	2	JT0959	polyprotein - pota
39	52.5	24.2	314	2	F86805	cation transporter
40	52.5	24.2	678	2	C86495	hypothetical prote
41	52.5	24.2	678	2	H72128	3-methyl-2-oxobuta
42	52	24.0	272	2	F70979	hypothetical prote
43	52	24.0	339	2	A81351	signal transductio
44	52	24.0	417	2	F70132	conserved hypothet
45	52	24.0	527	2	T18232	conserved hypothet

#### ALIGNMENTS

##### RESULT 1

PN0512

beta-amyloid protein - guinea pig (fragment)

C;Species: Cavia porcellus (guinea pig)

C;Date: 31-Dec-1993 #sequence\_revision 31-Dec-1993 #text\_change 17-Mar-1999

C;Accession: PN0512

R;Shimohigashi, Y.; Matsumoto, H.; Takano, Y.; Saito, R.; Iwata, T.; Kamiya, H.; Ohno, M.

Biochem. Biophys. Res. Commun. 193, 624-630, 1993

A;Title: Receptor-mediated specific biological activity of a beta-amyloid protein fragment for NK-1 substance p receptors.

A;Reference number: PN0512; MUID:93290653; PMID:7685598

A;Accession: PN0512

A;Molecule type: protein

A;Residues: 1-42 <SHI>

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; amyloid

Query Match

100.0%; Score 217; DB 2; Length 42;

Best Local Similarity 100.0%; Pred. No. 7.6e-22;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
          |||
Db      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
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#### RESULT 2

E60045

Alzheimer's disease amyloid beta/A4 protein precursor - sheep (fragment)

C;Species: Ovis sp. (sheep)

C;Date: 01-Dec-1992 #sequence\_revision 01-Dec-1992 #text\_change 28-Jul-1995

C;Accession: E60045

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: E60045

A;Molecule type: mRNA

A;Residues: 1-57 <JOH>

A;Cross-references: EMBL:X56130

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 217; DB 2; Length 57;  
Best Local Similarity 100.0%; Pred. No. 1.1e-21;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
          |||
Db      6 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 47
```

#### RESULT 3

F60045

Alzheimer's disease amyloid beta/A4 protein precursor - pig (fragment)

C;Species: Sus scrofa domestica (domestic pig)

C;Date: 01-Dec-1992 #sequence\_revision 01-Dec-1992 #text\_change 13-Aug-1999

C;Accession: F60045

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: F60045

A;Molecule type: mRNA

A;Residues: 1-57 <JOH>

A;Cross-references: EMBL:X56127; NID:g1895; PIDN:CAA39592.1; PID:g1896

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain





C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 217; DB 2; Length 57;  
Best Local Similarity 100.0%; Pred. No. 1.1e-21;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
|||||  
Db 6 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 47

RESULT 8

PQ0438

Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)

C;Species: *Oryctolagus cuniculus* (domestic rabbit)

C;Date: 30-Sep-1993 #sequence\_revision 19-Oct-1995 #text\_change 19-Oct-1995

C;Accession: PQ0438; C60045

R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.

Biochem. Biophys. Res. Commun. 188, 905-911, 1992

A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid precursor protein gene.

A;Reference number: PQ0438; MUID:93075180; PMID:1445331

A;Accession: PQ0438

A;Molecule type: DNA

A;Residues: 1-82 <DAV>

A;Cross-references: GB:M83558; GB:M83657

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: C60045

A;Molecule type: mRNA

A;Residues: 12-68 <JOH>

A;Cross-references: EMBL:X56129

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; Down's syndrome

Query Match 100.0%; Score 217; DB 2; Length 82;  
Best Local Similarity 100.0%; Pred. No. 1.6e-21;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
|||||  
Db 17 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 58

RESULT 9

A49795

Alzheimer's disease amyloid beta protein precursor - crab-eating macaque

C;Species: *Macaca fascicularis* (crab-eating macaque)

C;Date: 10-Sep-1999 #sequence\_revision 10-Sep-1999 #text\_change 10-Sep-1999

C;Accession: A49795

R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.

Am. J. Pathol. 138, 1423-1435, 1991



A;Title: Homology of the amyloid beta protein precursor in monkey and human supports a primate model for beta amyloidosis in Alzheimer's disease.  
A;Reference number: A49795; MUID:91273117; PMID:1905108  
A;Accession: A49795  
A;Status: preliminary  
A;Molecule type: mRNA  
A;Residues: 1-695 <POD>  
A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
C;Keywords: alternative splicing

Query Match 100.0%; Score 217; DB 1; Length 695;  
Best Local Similarity 100.0%; Pred. No. 1.6e-20;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
|||||  
Db 597 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 638

# RESULT 10

## QRHUA4

Alzheimer's disease amyloid beta protein precursor [validated] - human  
N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor XIa inhibitor; proteinase nexin II (PN-II)  
N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)  
C;Species: Homo sapiens (man)  
C;Date: 30-Jun-1987 #sequence\_revision 28-Jul-1995 #text\_change 15-Sep-2000  
C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038; S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644  
R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.  
Nucleic Acids Res. 17, 517-522, 1989  
A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.  
A;Reference number: S02260; MUID:89128427; PMID:2783775  
A;Accession: S02260  
A;Molecule type: DNA  
A;Residues: 1-288,'V',365-770 <LEM1>  
A;Cross-references: EMBL:X13466  
A;Note: alternative splice form APP(695)  
R;Lemaire, H.G.  
submitted to the EMBL Data Library, November 1988  
A;Reference number: S05194  
A;Accession: S05194  
A;Molecule type: DNA  
A;Residues: 1-14,'VW',17-288,'V',365-770 <LEM2>  
A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360  
A;Note: alternative splice form APP(695)  
R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.  
Biochem. Biophys. Res. Commun. 159, 297-304, 1989

A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.  
 A;Reference number: A32277; MUID:89165870; PMID:2538123  
 A;Accession: A32277  
 A;Molecule type: DNA  
 A;Residues: 1-75 <LAF>  
 A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1; PID:g516074  
 R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little, S.P.  
 Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989  
 A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows similarity to soybean trypsin inhibitor.  
 A;Reference number: A33260; MUID:89392030; PMID:2675837  
 A;Accession: A33260  
 A;Molecule type: DNA  
 A;Residues: 656-737 <JOH>  
 A;Cross-references: GB:M29270; NID:g178863; PIDN:AAA51768.1; PID:g178865  
 R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.; Frangione, B.  
 Biochem. Biophys. Res. Commun. 170, 301-307, 1990  
 A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein diagnostic assays.  
 A;Reference number: A35486; MUID:90321244; PMID:2196878  
 A;Accession: A35486  
 A;Molecule type: DNA  
 A;Residues: 672-710 <PRE1>  
 A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients  
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.  
 Gene 87, 257-263, 1990  
 A;Title: Genomic organization of the human amyloid beta-protein precursor gene.  
 A;Reference number: I39451; MUID:90236318; PMID:2110105  
 A;Accession: I39452  
 A;Status: nucleic acid sequence not shown; translation not shown; translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 1-770 <YOS1>  
 A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616  
 A;Accession: I39451  
 A;Status: nucleic acid sequence not shown; translation not shown; translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 1-530, 'QWLMPVIPAFWEAKVGR' <YOS2>  
 A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615  
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.  
 Gene 102, 291-292, 1991  
 A;Reference number: A59020; MUID:91340168; PMID:1908403  
 A;Contents: annotation; erratum  
 A;Note: revised physical map for reference I39451  
 R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.; van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.  
 Science 248, 1124-1126, 1990  
 A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral hemorrhage, Dutch type.  
 A;Reference number: I39453; MUID:90260663; PMID:2111584  
 A;Accession: I39453

A;Status: translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 656-737 <LEV>  
 A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620  
 A;Note: a mutation with 693-Gln is presented  
 R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.  
 Science 254, 97-99, 1991  
 A;Title: A mutation in the amyloid precursor protein associated with hereditary Alzheimer's disease.  
 A;Reference number: I59562; MUID:92022553; PMID:1925564  
 A;Accession: I59562  
 A;Status: translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 689-716,'F',718-737 <MUR>  
 A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721  
 R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.; Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.; Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma, V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.; Schellenberg, G.D.  
 Am. J. Hum. Genet. 51, 998-1014, 1992  
 A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds for the APP gene region.  
 A;Reference number: A44017; MUID:93035397; PMID:1415269  
 A;Accession: A44017  
 A;Molecule type: DNA  
 A;Residues: 687-692,'G',694-718 <KAM1>  
 A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378  
 A;Experimental source: familial Alzheimer disease family SB  
 A;Note: sequence extracted from NCBI backbone (NCBIP:115374)  
 A;Accession: B44017  
 A;Molecule type: DNA  
 A;Residues: 687-718 <KAM2>  
 A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380  
 A;Experimental source: familial Alzheimer disease family LIT  
 A;Note: sequence extracted from NCBI backbone (NCBIP:115376)  
 A;Note: this sequence has a silent mutation  
 R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.; Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B.  
 Nature 325, 733-736, 1987  
 A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor.  
 A;Reference number: A03134; MUID:87144572; PMID:2881207  
 A;Accession: A03134  
 A;Molecule type: mRNA  
 A;Residues: 1-288,'V',365-770 <KAN>  
 A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526  
 A;Note: alternative splice form APP(695)  
 R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M.  
 Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987  
 A;Title: Molecular cloning and characterization of a cDNA encoding the cerebrovascular and the neuritic plaque amyloid peptides.  
 A;Reference number: A29030; MUID:87231971; PMID:3035574  
 A;Accession: A29030  
 A;Molecule type: mRNA  
 A;Residues: 284-288,'V',365-646,'E',648-770 <ROB>  
 A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540

A;Note: the authors translated the codon GAG for residue 647 as Asp  
 R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C.  
 Science 235, 877-880, 1987  
 A;Title: Characterization and chromosomal localization of a cDNA encoding brain  
 amyloid of Alzheimer's disease.  
 A;Reference number: A47584; MUID:87120328; PMID:3810169  
 A;Accession: A47584  
 A;Molecule type: mRNA  
 A;Residues: 674-756,'S',758-770 <GOL>  
 A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707  
 A;Experimental source: brain  
 R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop,  
 P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L.  
 Science 235, 880-884, 1987  
 A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage  
 near the Alzheimer locus.  
 A;Reference number: A47585; MUID:87120329; PMID:2949367  
 A;Accession: A47585  
 A;Molecule type: mRNA  
 A;Residues: 674-703 <TAN1>  
 A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958  
 R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang,  
 J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K.  
 EMBO J. 7, 949-957, 1988  
 A;Title: Identification, transmembrane orientation and biogenesis of the amyloid  
 A4 precursor of Alzheimer's disease.  
 A;Reference number: S02638; MUID:88296437; PMID:2900137  
 A;Accession: S02638  
 A;Molecule type: mRNA  
 A;Residues: 672-678 <DYR>  
 R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella,  
 J.F.; Neve, R.L.  
 Nature 331, 528-530, 1988  
 A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA  
 associated with Alzheimer's disease.  
 A;Reference number: S00707; MUID:88122640; PMID:2893290  
 A;Accession: S00707  
 A;Molecule type: mRNA  
 A;Residues: 286-344,'I',365-366 <TAN2>  
 A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612  
 A;Experimental source: promyelocytic leukemia cell line HL60  
 A;Note: alternative splice form APP(751)  
 R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.;  
 Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.  
 Nature 331, 525-527, 1988  
 A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase  
 inhibitors.  
 A;Reference number: S00925; MUID:88122639; PMID:2893289  
 A;Accession: S00925  
 A;Molecule type: mRNA  
 A;Residues: 1-344,'I',365-770 <PO2>  
 A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1;  
 PID:g28721  
 A;Note: alternative splice form APP(751)  
 R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.  
 Nature 331, 530-532, 1988

A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.  
A;Reference number: A38949; MUID:88122641; PMID:2893291  
A;Accession: A38949  
A;Molecule type: mRNA  
A;Residues: 287-367 <KIT>  
A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611  
A;Experimental source: glioblastoma cell line  
A;Note: alternative splice form APP(770)  
R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer, B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.  
Brain Res. Mol. Brain Res. 4, 121-131, 1988  
A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of three patients with sporadic Alzheimer's disease.  
A;Reference number: A30320  
A;Accession: A30320  
A;Status: not compared with conceptual translation  
A;Molecule type: mRNA  
A;Residues: 284-288,'V',365-770 <VIT1>  
A;Accession: B30320  
A;Status: not compared with conceptual translation  
A;Molecule type: mRNA  
A;Residues: 122-288,'V',365-770 <VIT2>  
A;Accession: C30320  
A;Status: not compared with conceptual translation  
A;Molecule type: mRNA  
A;Residues: 606-770 <VIT3>  
R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.; Marotta, C.A.  
Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988  
A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer disease brain: coding and noncoding regions of the fetal precursor mRNA are expressed in the cortex.  
A;Reference number: A31087; MUID:88124954; PMID:2893379  
A;Accession: A31087  
A;Molecule type: mRNA  
A;Residues: 507-770 <ZAI>  
A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573  
A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn, AAT for residue 610 as Gly, and GGT for residue 655 as Ser  
A;Note: the cited Genbank accession number, J03594, is not in release 101.0  
R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.; Beyreuther, K.

RESULT 11  
A27485

Alzheimer's disease amyloid beta/A4 protein homolog precursor - mouse  
N;Alternate names: proteinase nexin II  
C;Species: Mus musculus (house mouse)  
C;Date: 31-Mar-1989 #sequence\_revision 31-Mar-1989 #text\_change 13-Aug-1999  
C;Accession: A27485; S19727; I49485  
R;Yamada, T.; Sasaki, H.; Furuya, H.; Miyata, T.; Goto, I.; Sakaki, Y.  
Biochem. Biophys. Res. Commun. 149, 665-671, 1987  
A;Title: Complementary DNA for the mouse homolog of the human amyloid beta protein precursor.  
A;Reference number: A27485; MUID:88106489; PMID:3322280  
A;Accession: A27485  
A;Molecule type: mRNA  
A;Residues: 1-695 <YAM>  
A;Cross-references: GB:M18373; NID:g191568; PIDN:AAA37139.1; PID:g309085  
A;Experimental source: brain  
R;de Strooper, B.; van Leuven, F.; van den Berghe, H.  
Biochim. Biophys. Acta 1129, 141-143, 1991  
A;Title: The amyloid beta protein precursor or proteinase nexin II from mouse is closer related to its human homolog than previously reported.  
A;Reference number: S19727; MUID:92096458; PMID:1756177  
A;Accession: S19727  
A;Molecule type: mRNA  
A;Residues: 1-210,'G',212-220,'S',222-396,'A',398-402,'T',404-448,'A',450-695  
<STR>  
A;Cross-references: EMBL:X59379  
R;Izumi, R.; Yamada, T.; Yoshikai, S.; Sasaki, H.; Hattori, M.; Sakaki, Y.  
Gene 112, 189-195, 1992  
A;Title: Positive and negative regulatory elements for the expression of the Alzheimer's disease amyloid precursor-encoding gene in mouse.  
A;Reference number: I49485; MUID:92209998; PMID:1555768  
A;Accession: I49485  
A;Status: translated from GB/EMBL/DDBJ  
A;Molecule type: DNA  
A;Residues: 1-19 <RES>  
A;Cross-references: GB:D10603; NID:g220328; PIDN:BAA01456.1; PID:g220329  
C;Genetics:  
A;Map position: 16C3  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid; transmembrane protein

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Matches 39; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

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Db 597 DAEFGHDSGFVVRHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 638

RESULT 12  
S00550

Alzheimer's disease amyloid beta protein precursor - rat  
N;Alternate names: beta-A4 amyloid protein  
C;Species: Rattus norvegicus (Norway rat)  
C;Date: 30-Jun-1989 #sequence\_revision 30-Jun-1989 #text\_change 13-Aug-1999  
C;Accession: S00550; A41245; A39820; S46251

R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.; Seeburg, P.H.  
EMBO J. 7, 1365-1370, 1988  
A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact.  
A;Reference number: S00550; MUID:88312583; PMID:2900758  
A;Accession: S00550  
A;Molecule type: mRNA  
A;Residues: 1-695 <SHI>  
A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617  
R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.  
Science 241, 223-226, 1988  
A;Title: Amyloid beta protein precursor is possibly a heparan sulfate proteoglycan core protein.  
A;Reference number: A41245; MUID:88264430; PMID:2968652  
A;Accession: A41245  
A;Molecule type: protein  
A;Residues: 18-37, 'X', 39-40, 'X', 42-44 <SCH>  
A;Note: evidence for heparan sulfate attachment  
R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.  
FEBS Lett. 349, 109-116, 1994  
A;Title: The beta-A4 amyloid precursor protein binding to copper.  
A;Reference number: S46251; MUID:94320627; PMID:7913895  
A;Contents: annotation; copper binding sites  
A;Note: rat peptides were isolated but not sequenced  
R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.  
J. Biol. Chem. 266, 8464-8469, 1991  
A;Title: Purification and tissue level of the beta-amyloid peptide precursor of rat brain.  
A;Reference number: A39820; MUID:91217087; PMID:1673681  
A;Accession: A39820  
A;Status: preliminary  
A;Molecule type: protein  
A;Residues: 18-32 <POT>  
A;Experimental source: brain  
C;Comment: Deposition of amyloid protein as neurofibrillary tangles and/or plaques is characteristic of both Alzheimer's disease and Down's syndrome.  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid; glycoprotein; transmembrane protein  
F;625-648/Domain: transmembrane #status predicted <TMM>

Query Match 91.2%; Score 198; DB 2; Length 695;  
Best Local Similarity 92.9%; Pred. No. 5.2e-18;  
Matches 39; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
||||| :||| |||||  
Db 597 DAEFGHDSGFEVRHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 638

RESULT 13

JH0773

Alzheimer's disease amyloid beta protein precursor - African clawed frog

C;Species: Xenopus laevis (African clawed frog)

C;Date: 10-Jun-1993 #sequence\_revision 10-Jun-1993 #text\_change 13-Aug-1999

C;Accession: JH0773

R;Okado, H.; Okamoto, H.  
Biochem. Biophys. Res. Commun. 189, 1561-1568, 1992  
A;Title: A *Xenopus* homologue of the human beta-amyloid precursor protein:  
developmental regulation of its gene expression.  
A;Reference number: JH0773; MUID:93129227; PMID:1282805  
A;Accession: JH0773  
A;Molecule type: mRNA  
A;Residues: 1-747 <OKA>  
A;Cross-references: GB:S52417; NID:g263150; PIDN:AAB24853.1; PID:g263151  
A;Experimental source: larva  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid  
F;287-337/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Qy            1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA    42  
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RESULT 15
AI3228
tryptophan 2-monooxygenase tms1 [imported] - Agrobacterium tumefaciens (strain
C58, Dupont) plasmid Ti
C;Species: Agrobacterium tumefaciens
C;Date: 11-Jan-2002 #sequence_revision 11-Jan-2002 #text_change 18-Nov-2002
C;Accession: AI3228

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R;Wood, D.W.; Setubal, J.C.; Kaul, R.; Monks, D.; Chen, L.; Wood, G.E.; Chen, Y.; Woo, L.; Kitajima, J.P.; Okura, V.K.; Almeida Jr., N.F.; Zhou, Y.; Bovee Sr., D.; Chapman, P.; Clendenning, J.; Deatherage, G.; Gillet, W.; Grant, C.; Guenther, D.; Kutayavin, T.; Levy, R.; Li, M.; McClelland, E.; Palmieri, A.; Raymond, C.; Rouse, G.; Saenphimmachak, C.; Wu, Z.; Gordon, D.; Eisen, J.A.; Paulsen, I.; Karp, P.; Romero, P.; Zhang, S.

Science 294, 2317-2323, 2001

A;Authors: Yoo, H.; Tao, Y.; Biddle, P.; Jung, M.; Krespan, W.; Perry, M.; Gordon-Kamm, B.; Liao, L.; Kim, S.; Hendrick, C.; Zhao, Z.; Dolan, M.; Tingey, S.V.; Tomb, J.; Gordon, M.P.; Olson, M.V.; Nester, E.W.

A;Title: The Genome of the Natural Genetic Engineer *Agrobacterium tumefaciens* C58.

A;Reference number: AB2577; MUID:21608550; PMID:11743193

A;Accession: AI3228

A;Status: preliminary

A;Molecule type: DNA

A;Residues: 1-755 <KUR>

A;Cross-references: GB:AE008690; PIDN:AAL46247.1; PID:g17744025; GSPDB:GN00189

A;Experimental source: strain C58 (Dupont)

C;Genetics:

A;Gene: tms1

A;Genome: plasmid

C;Superfamily: *Agrobacterium* plasmid tryptophan 2-monooxygenase

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Db 223 DSG-----RIGFFPEDVPKPKVAIIGAGISGLVVA 252

Search completed: July 15, 2004, 18:04:44

Job time : 18 secs

GenCore version 5.1.6  
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OM protein - protein search, using sw model

Run on: July 15, 2004, 18:04:19 ; Search time 46 Seconds  
(without alignments)  
285.381 Million cell updates/sec

Title: US-09-724-940-42  
Perfect score: 217  
Sequence: 1 DAEFRHDSGYEVHHQKLVFF.....DVGSNKGAIIGLMVGGVVIA 42

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1285345 seqs, 312560633 residues

Total number of hits satisfying chosen parameters: 1285345

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

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3: /cgn2\_6/ptodata/1/pubpaa/US06\_NEW\_PUB.pep:\*  
4: /cgn2\_6/ptodata/1/pubpaa/US06\_PUBCOMB.pep:\*  
5: /cgn2\_6/ptodata/1/pubpaa/US07\_NEW\_PUB.pep:\*  
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7: /cgn2\_6/ptodata/1/pubpaa/US08\_NEW\_PUB.pep:\*  
8: /cgn2\_6/ptodata/1/pubpaa/US08\_PUBCOMB.pep:\*  
9: /cgn2\_6/ptodata/1/pubpaa/US09A\_PUBCOMB.pep:\*  
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13: /cgn2\_6/ptodata/1/pubpaa/US10A\_PUBCOMB.pep:\*  
14: /cgn2\_6/ptodata/1/pubpaa/US10B\_PUBCOMB.pep:\*  
15: /cgn2\_6/ptodata/1/pubpaa/US10C\_PUBCOMB.pep:\*  
16: /cgn2\_6/ptodata/1/pubpaa/US10\_NEW\_PUB.pep:\*  
17: /cgn2\_6/ptodata/1/pubpaa/US60\_NEW\_PUB.pep:\*  
18: /cgn2\_6/ptodata/1/pubpaa/US60\_PUBCOMB.pep:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

SUMMARIES

Result  
No.      Score      Match Length DB      ID      Description

1	217	100.0	42	8	US-08-923-055-2	Sequence 2, Appli
2	217	100.0	42	9	US-09-867-847-1	Sequence 1, Appli
3	217	100.0	42	9	US-09-956-625-26	Sequence 26, Appl
4	217	100.0	42	9	US-09-731-460-1	Sequence 1, Appli
5	217	100.0	42	10	US-09-962-955C-37	Sequence 37, Appl
6	217	100.0	42	10	US-09-848-616-174	Sequence 174, App
7	217	100.0	42	10	US-09-865-294-65	Sequence 65, Appl
8	217	100.0	42	10	US-09-792-079-13	Sequence 13, Appl
9	217	100.0	42	10	US-09-825-242-1	Sequence 1, Appli
10	217	100.0	42	10	US-09-930-915A-293	Sequence 293, App
11	217	100.0	42	12	US-10-337-261-2	Sequence 2, Appli
12	217	100.0	42	12	US-10-363-082-1	Sequence 1, Appli
13	217	100.0	42	12	US-10-433-385-6	Sequence 6, Appli
14	217	100.0	42	12	US-10-231-063C-15	Sequence 15, Appl
15	217	100.0	42	12	US-10-455-218-2	Sequence 2, Appli
16	217	100.0	42	12	US-10-423-047-1	Sequence 1, Appli
17	217	100.0	42	13	US-10-051-496-2	Sequence 2, Appli
18	217	100.0	42	13	US-10-082-804-7	Sequence 7, Appli
19	217	100.0	42	14	US-10-217-584-2	Sequence 2, Appli
20	217	100.0	42	14	US-10-169-580-2	Sequence 2, Appli
21	217	100.0	42	14	US-10-278-181-1	Sequence 1, Appli
22	217	100.0	42	14	US-10-143-534-2	Sequence 2, Appli
23	217	100.0	42	14	US-10-190-548A-1	Sequence 1, Appli
24	217	100.0	42	14	US-10-051-663-2	Sequence 2, Appli
25	217	100.0	42	14	US-10-159-279-13	Sequence 13, Appl
26	217	100.0	42	14	US-10-050-902-220	Sequence 220, App
27	217	100.0	42	14	US-10-050-898-220	Sequence 220, App
28	217	100.0	42	14	US-10-082-014-81	Sequence 81, Appl
29	217	100.0	42	14	US-10-372-076-82	Sequence 82, Appl
30	217	100.0	42	15	US-10-231-298B-15	Sequence 15, Appl
31	217	100.0	42	15	US-10-231-470C-15	Sequence 15, Appl
32	217	100.0	42	15	US-10-366-125-28	Sequence 28, Appl
33	217	100.0	42	15	US-10-411-544-2	Sequence 2, Appli
34	217	100.0	42	15	US-10-231-213D-15	Sequence 15, Appl
35	217	100.0	42	15	US-10-231-114C-15	Sequence 15, Appl
36	217	100.0	42	16	US-10-617-876-7	Sequence 7, Appli
37	217	100.0	42	16	US-10-429-216-1	Sequence 1, Appli
38	217	100.0	42	16	US-10-656-624-5	Sequence 5, Appli
39	217	100.0	43	9	US-09-280-966-1	Sequence 1, Appli
40	217	100.0	43	9	US-09-904-987-1	Sequence 1, Appli
41	217	100.0	43	9	US-09-808-037-3	Sequence 3, Appli
42	217	100.0	43	9	US-09-866-712-3	Sequence 3, Appli
43	217	100.0	43	9	US-09-972-475-1	Sequence 1, Appli
44	217	100.0	43	9	US-09-992-800-1	Sequence 1, Appli
45	217	100.0	43	9	US-09-895-443-1	Sequence 1, Appli

#### ALIGNMENTS

RESULT 1  
 US-08-923-055-2  
 ; Sequence 2, Application US/08923055  
 ; Publication No. US20010016327A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Dana Giulian

```

; TITLE OF INVENTION: Identification of Agents that Protect
; TITLE OF INVENTION: Against Inflammatory Injury to Neurons
; NUMBER OF SEQUENCES: 2
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Woodcock Washburn Kurtz Mackiewicz
; ADDRESSEE: & No. US20010016327Alris LLP
; STREET: One Liberty Place - 46th Floor
; CITY: Philadelphia
; STATE: PA
; COUNTRY: USA
; ZIP: 19103
; COMPUTER READABLE FORM:
; MEDIUM TYPE: DISKETTE, 3.5 INCH, 1.44 Mb STORAGE
; COMPUTER: IBM PS/2
; OPERATING SYSTEM: PC-DOS
; SOFTWARE: WORDPERFECT for WINDOWS 6.0
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/923,055
; FILING DATE: Sept-03-97
; CLASSIFICATION: 435
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER:
; FILING DATE:
; ATTORNEY/AGENT INFORMATION:
; NAME: Lori Y. Beardell
; REGISTRATION NUMBER: 34,293
; REFERENCE/DOCKET NUMBER: BYLR-0038
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (215) 568-3100
; TELEFAX: (215) 568-3439~
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 42 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: peptide
US-08-923-055-2

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Query Match          100.0%; Score 217; DB 8; Length 42;
Best Local Similarity 100.0%; Pred. No. 5e-23;
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
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Db      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

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## RESULT 2

US-09-867-847-1

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; Sequence 1, Application US/09867847
; Patent No. US20020094335A1
; GENERAL INFORMATION:
; APPLICANT: Chalifour, Robert
; APPLICANT: Hebert, Lise
; APPLICANT: Kong, Xianqi
; APPLICANT: Gervais, Francine
; TITLE OF INVENTION: VACCINE FOR THE PREVENTION AND TREATMENT OF ALZHEIMER'S

```



RESULT 4

US-09-731-460-1

; Sequence 1, Application US/09731460  
 ; Patent No. US20020137112A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Chojkier, Mario  
 ; APPLICANT: Buck, Martina  
 ; TITLE OF INVENTION: Compositions and Methods for Diagnosing Alzheimer's  
 ; TITLE OF INVENTION: Disease  
 ; FILE REFERENCE: CHOJKIER-04302  
 ; CURRENT APPLICATION NUMBER: US/09/731,460  
 ; CURRENT FILING DATE: 2000-12-07  
 ; NUMBER OF SEQ ID NOS: 1  
 ; SOFTWARE: PatentIn Ver. 2.0  
 ; SEQ ID NO 1  
 ; LENGTH: 42  
 ; TYPE: PRT  
 ; ORGANISM: Artificial Sequence  
 ; FEATURE:  
 ; OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 US-09-731-460-1

Query Match 100.0%; Score 217; DB 9; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 5e-23;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 5

US-09-962-955C-37

; Sequence 37, Application US/09962955C  
 ; Publication No. US20030013648A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Gerardo M. Castillo  
 ; APPLICANT: Alan D. Snow  
 ; NUMBER OF SEQUENCES: 37  
 ; CORRESPONDENCE ADDRESS:  
 ; ADDRESSEE: Patrick M. Dwyer  
 ; STREET: ProteoTech, Inc, 1818 Westlake Avenue N, Suite 114  
 ; CITY: Seattle  
 ; STATE: WA (Washington)  
 ; COUNTRY: United States of America  
 ; ZIP: 98109  
 ; COMPUTER READABLE FORM:  
 ; MEDIUM TYPE: Diskette - 3.50 inch, 1.44 Mb storage  
 ; COMPUTER: IBM PC  
 ; OPERATING SYSTEM: Windows 98  
 ; SOFTWARE: WordPerfect 9  
 ; CURRENT APPLICATION DATA:  
 ; APPLICATION NUMBER: US/09/962,955C  
 ; FILING DATE: 24-September-2001  
 ; CLASSIFICATION:  
 ; PRIOR APPLICATION DATA:  
 ; APPLICATION NUMBER: 09/938,275

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; FILING DATE: 22-August-2001
; CLASSIFICATION:
; ATTORNEY/AGENT INFORMATION:
; NAME: Dwyer, Patrick M.
; REGISTRATION NUMBER: 32,411
; REFERENCE/DOCKET NUMBER: PROTEO.P03CI
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (206) 343-7074
; TELEFAX: (206) 343-7085
; INFORMATION FOR SEQ ID NO: 37:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 42 AMINO ACIDS
; TYPE: AMINO ACID
; STRANDEDNESS:
; TOPOLOGY: LINEAR
; ORIGINAL SOURCE:
; ORGANISM: MOUSE
; FEATURE:
; OTHER INFORMATION: Also referred to in the specification as "AB 1-42"
US-09-962-955C-37

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Query Match          100.0%; Score 217; DB 10; Length 42;
Best Local Similarity 100.0%; Pred. No. 5e-23;
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

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# RESULT 6

```

US-09-848-616-174
; Sequence 174, Application US/09848616
; Publication No. US20030054010A1
; GENERAL INFORMATION:
; APPLICANT: Sebbel, Peter
; APPLICANT: Dunant, Nicolas
; APPLICANT: Bachmann, Martin
; APPLICANT: Tissot, Alain
; APPLICANT: Lechner, Franziska
; TITLE OF INVENTION: Molecular Antigen Array
; FILE REFERENCE: 1700.0180002
; CURRENT APPLICATION NUMBER: US/09/848,616
; CURRENT FILING DATE: 2001-05-05
; NUMBER OF SEQ ID NOS: 186
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 174
; LENGTH: 42
; TYPE: PRT
; ORGANISM: Unknown
; FEATURE:
; OTHER INFORMATION: Amyloid Beta Peptide
US-09-848-616-174

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Query Match          100.0%; Score 217; DB 10; Length 42;
Best Local Similarity 100.0%; Pred. No. 5e-23;
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
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Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

## RESULT 7

US-09-865-294-65

; Sequence 65, Application US/09865294

; Publication No. US20030068325A1

; GENERAL INFORMATION:

; APPLICANT: Wang, Chang Yi

; TITLE OF INVENTION: Immunogenic peptide composition as vaccines for the

; TITLE OF INVENTION: prevention and treatment of Alzheimer's Disease

; FILE REFERENCE: 1151-4167

; CURRENT APPLICATION NUMBER: US/09/865,294

; CURRENT FILING DATE: 2001-05-25

; NUMBER OF SEQ ID NOS: 76

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; SOFTWARE: PatentIn Ver. 2.0
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; SEQ ID NO 65

; LENGTH: 42

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; TYPE: PRT
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; ORGANISM: Homo sapiens

US-09-865-294-65

Query Match 100.0%; Score 217; DB 10; Length 42;

Best Local Similarity 100.0%; Pred. No. 5e-23;

Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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 |||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

## RESULT 8

US-09-792-079-13

; Sequence 13, Application US/09792079

; Publication No. US20030083277A1

; GENERAL INFORMATION:

; APPLICANT: University of Kentucky Research Foundation

APPLICANT: Hersh, Louis B.

; APPLICANT: Mukherjee, Atish

10 TITLE OF INVENTION: Use Of Insulin Degrading Enzyme (IDE) For The Treatment

## Of Alzheimer's

; TITLE OF INVENTION: Disease Patients

; FILE REFERENCE: 050229-0261

; CURRENT APPLICATION NUMBER: US/09/792,079

; CURRENT FILING DATE: 2001-02-26

: PRIOR APPLICATION NUMBER: 60/184.826

: PRIOR FILING DATE: 2000-02-24

; NUMBER OF SEO ID NOS: 13

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: SOFTWARE: PatentIn version 3.1

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: SEQ ID NO 13

: LENGTH: 42

TYPE: PRT

: ORGANISM: Homo sapiens

US-09-792-079-13









RESULT 14

US-10-231-063C-15

; Sequence 15, Application US/10231063C  
 ; Publication No. US20030224476A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Chou, Szu-Yi  
 ; TITLE OF INVENTION: Method of Producing Transglutaminase Reactive Compound  
 ; FILE REFERENCE: SAMG/0004  
 ; CURRENT APPLICATION NUMBER: US/10/231,063C  
 ; CURRENT FILING DATE: 2002-08-28  
 ; PRIOR APPLICATION NUMBER: 60/361,166  
 ; PRIOR FILING DATE: 2002-03-01  
 ; PRIOR APPLICATION NUMBER: 60/363,445  
 ; PRIOR FILING DATE: 2002-03-08  
 ; NUMBER OF SEQ ID NOS: 16  
 ; SOFTWARE: PatentIn version 3.1  
 ; SEQ ID NO 15  
 ; LENGTH: 42  
 ; TYPE: PRT  
 ; ORGANISM: Homo sapiens  
 US-10-231-063C-15

Query Match 100.0%; Score 217; DB 12; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 5e-23;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||||  
 Db 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42

RESULT 15

US-10-455-218-2

; Sequence 2, Application US/10455218  
 ; Publication No. US20030204051A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Glabe, Charles  
 ; APPLICANT: Garzon-Rodriguez, William  
 ; TITLE OF INVENTION: FLUORESCENT AMYLOID ABETA PEPTIDES AND  
 ; TITLE OF INVENTION: USES THEREOF  
 ; FILE REFERENCE: 50016/002002  
 ; CURRENT APPLICATION NUMBER: US/10/455,218  
 ; CURRENT FILING DATE: 2003-06-05  
 ; PRIOR APPLICATION NUMBER: US/09/133,866  
 ; PRIOR FILING DATE: 1998-08-13  
 ; PRIOR APPLICATION NUMBER: EARLIER APPLICATION NUMBER: 60/055,660  
 ; PRIOR FILING DATE: EARLIER FILING DATE: 1997-08-14  
 ; NUMBER OF SEQ ID NOS: 2  
 ; SOFTWARE: FastSEQ for Windows Version 3.0  
 ; SEQ ID NO 2  
 ; LENGTH: 42  
 ; TYPE: PRT  
 ; ORGANISM: Homo sapiens  
 US-10-455-218-2

Query Match 100.0%; Score 217; DB 12; Length 42;  
 Best Local Similarity 100.0%; Pred. No. 5e-23;

Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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          |||||||||||||||||||||||||||||||||||||||
Db      1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42
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Search completed: July 15, 2004, 18:09:47  
Job time : 48 secs

GenCore version 5.1.6  
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 15, 2004, 17:59:53 ; Search time 36 Seconds  
(without alignments)  
368.105 Million cell updates/sec

Title: US-09-724-940-42  
Perfect score: 217  
Sequence: 1 DAEFRHDSGYEVHHQKLVFF.....DVGSNKGAIIGLMVGGVVIA 42

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1017041 seqs, 315518202 residues

Total number of hits satisfying chosen parameters: 1017041

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : SPTREMBL\_25:\*  
1: sp\_archaea:\*  
2: sp\_bacteria:\*  
3: sp\_fungi:\*  
4: sp\_human:\*  
5: sp\_invertebrate:\*  
6: sp\_mammal:\*  
7: sp\_mhc:\*  
8: sp\_organelle:\*  
9: sp\_phage:\*  
10: sp\_plant:\*  
11: sp\_rodent:\*  
12: sp\_virus:\*  
13: sp Vertebrate:\*  
14: sp\_unclassified:\*  
15: sp\_rvirus:\*  
16: sp\_bacteriap:\*  
17: sp\_archeap:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result	%	Query					
No.	Score	Match	Length	DB	ID	Description	
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1	217	100.0	82	4	Q16020	Q16020 homo sapien
2	217	100.0	82	4	Q16014	Q16014 homo sapien
3	217	100.0	82	4	Q16019	Q16019 homo sapien
4	217	100.0	113	13	Q8JH58	Q8jh58 chelydra se
5	217	100.0	534	13	O93296	O93296 gallus gall
6	217	100.0	569	13	Q9PVL1	Q9pvl1 gallus gall
7	217	100.0	695	13	Q9DGJ8	Q9dgj8 gallus gall
8	217	100.0	751	13	Q9DGJ7	Q9dgj7 gallus gall
9	198	91.2	79	11	O35463	O35463 cricetulus
10	198	91.2	218	11	Q8BPV5	Q8bpv5 mus musculu
11	198	91.2	384	11	Q8BPC7	Q8bpc7 mus musculu
12	198	91.2	693	13	Q98SG0	Q98sg0 xenopus lae
13	198	91.2	747	13	Q91963	Q91963 xenopus. ap
14	195	89.9	695	13	Q98SF9	Q98sf9 xenopus lae
15	195	89.9	695	13	Q7ZXQ0	Q7zxq0 xenopus lae
16	188	86.6	699	13	O57394	O57394 narke japon
17	176	81.1	33	4	Q9UC33	Q9uc33 homo sapien
18	162	74.7	30	4	Q9UCA9	Q9uca9 homo sapien
19	157.5	72.6	357	13	Q8UUI8	Q8uui8 brachydanio
20	157.5	72.6	472	13	Q8UUS0	Q8uus0 brachydanio
21	157.5	72.6	612	13	Q9I9E7	Q9i9e7 brachydanio
22	157.5	72.6	678	13	Q7ZZT1	Q7zzt1 brachydanio
23	157.5	72.6	738	13	Q90W28	Q90w28 brachydanio
24	156	71.9	239	13	Q8UUI7	Q8uui7 brachydanio
25	156	71.9	694	13	Q8UUR9	Q8uur9 brachydanio
26	147	67.7	28	4	Q9UCD1	Q9ucd1 homo sapien
27	121	55.8	49	6	O97917	O97917 bos taurus
28	106	48.8	19	4	Q9UCC8	Q9ucc8 homo sapien
29	95	43.8	35	4	Q8WZ99	Q8wz99 homo sapien
30	64	29.5	328	16	Q9RPS4	Q9rps4 enterococcu
31	63	29.0	321	16	Q8RG41	Q8rg41 fusobacteri
32	63	29.0	755	2	Q9R717	Q9r717 agrobacteri
33	63	29.0	755	2	Q9R472	Q9r472 agrobacteri
34	63	29.0	755	2	Q9R694	Q9r694 agrobacteri
35	63	29.0	755	16	Q8U6A3	Q8u6a3 agrobacteri
36	62	28.6	755	2	Q44388	Q44388 agrobacteri
37	60	27.6	351	7	Q8HWH7	Q8hwh7 squalus aca
38	60	27.6	755	2	Q9WWA1	Q9wwa1 agrobacteri
39	60	27.6	3336	5	Q8IKE1	Q8ikel plasmodium
40	58	26.7	368	16	Q8G2C8	Q8g2c8 brucella su
41	57.5	26.5	895	10	Q9AWB6	Q9awb6 lycopersico
42	57	26.3	195	10	O22662	O22662 arabidopsis
43	57	26.3	332	12	Q9DQN5	Q9dqn5 potato viru
44	57	26.3	337	12	Q8JPW2	Q8jpw2 potato viru
45	57	26.3	365	12	Q9WG05	Q9wg05 potato viru

# ALIGNMENTS

## RESULT 1

Q16020

ID Q16020 PRELIMINARY; PRT; 82 AA.  
AC Q16020;  
DT 01-NOV-1996 (TrEMBLrel. 01, Created)  
DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)  
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

DE Beta-amyloid peptide (Fragment).  
 GN BETA APP.  
 OS Homo sapiens (Human).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.  
 OX NCBI\_TaxID=9606;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=93236601; PubMed=8476439;  
 RA Denman R.B., Rosenzwaig R., Miller D.L.;  
 RT "A system for studying the effect(s) of familial Alzheimer disease  
 RT mutations on the processing of the beta-amyloid peptide precursor.";  
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).  
 DR EMBL; S61383; AAB26265.2; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF03494; Beta-APP; 1.  
 FT NON\_TER 1 1  
 FT NON\_TER 82 82  
 SQ SEQUENCE 82 AA; 8882 MW; F534AA5AE5D9230A CRC64;  
  
 Query Match 100.0%; Score 217; DB 4; Length 82;  
 Best Local Similarity 100.0%; Pred. No. 8.4e-21;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
  
 Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||||||  
 Db 18 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 59

RESULT 2

Q16014

ID Q16014 PRELIMINARY; PRT; 82 AA.  
 AC Q16014;  
 DT 01-NOV-1996 (TrEMBLrel. 01, Created)  
 DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Beta-amyloid peptide (Fragment).  
 OS Homo sapiens (Human).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.  
 OX NCBI\_TaxID=9606;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=93236601; PubMed=8476439;  
 RA Denman R.B., Rosenzwaig R., Miller D.L.;  
 RT "A system for studying the effect(s) of familial Alzheimer disease  
 RT mutations on the processing of the beta-amyloid peptide precursor.";  
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).  
 DR EMBL; S60721; AAB26263.2; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF03494; Beta-APP; 1.  
 FT NON\_TER 1 1  
 FT NON\_TER 82 82





OS Chelydra serpentina serpentina (common snapping turtle).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Testudines; Cryptodira; Testudinoidea; Chelydridae; Chelydra.  
 OX NCBI\_TaxID=134619;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=21876906; PubMed=11882478;  
 RA Trudeau V.L., Chiu S., Kennedy S.W., Brooks R.J.;  
 RT "Octylphenol (OP) alters the expression of members of the amyloid  
 RT protein family in the hypothalamus of the snapping turtle, Chelydra  
 RT serpentina serpentina.";  
 RL Environ. Health Perspect. 110:269-275(2002).  
 DR EMBL; AF541917; AAN04908.1; -.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 FT NON\_TER 1 1  
 SQ SEQUENCE 113 AA; 12750 MW; 72515C930496E053 CRC64;

Query Match 100.0%; Score 217; DB 13; Length 113;  
 Best Local Similarity 100.0%; Pred. No. 1.2e-20;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||||  
 Db 15 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 56

RESULT 5  
 O93296

ID O93296 . PRELIMINARY; PRT; 534 AA.  
 AC O93296;  
 DT 01-NOV-1998 (TrEMBLrel. 08, Created)  
 DT 01-NOV-1998 (TrEMBLrel. 08, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Amyloid protein (Fragment).  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98337885; PubMed=9671674;  
 RA Barnes N.Y., Li L., Yoshikawa K., Schwartz L.M., Oppenheim R.W.,  
 RA Milligan C.E.;  
 RT "Increased production of amyloid precursor protein provides a  
 RT substrate for caspase-3 in dying motoneurons.";  
 RL J. Neurosci. 18:5869-5880(1998).  
 DR EMBL; AF042098; AAC25052.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.

DR InterPro; IPR001255; Beta-APP.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR Pfam; PF03494; Beta-APP; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
FT NON\_TER 1 1  
SQ SEQUENCE 534 AA; 60597 MW; FB53ECC2E66D4C92 CRC64;

Query Match 100.0%; Score 217; DB 13; Length 534;  
Best Local Similarity 100.0%; Pred. No. 6.9e-20;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
|||||  
Db 436 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 477

# RESULT 6

## Q9PVL1

ID Q9PVL1 PRELIMINARY; PRT; 569 AA.  
AC Q9PVL1;  
DT 01-MAY-2000 (TrEMBLrel. 13, Created)  
DT 01-MAY-2000 (TrEMBLrel. 13, Last sequence update)  
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
DE Amyloid protein (Fragment).  
GN APP.  
OS Gallus gallus (Chicken).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
OC Gallus.  
OX NCBI\_TaxID=9031;  
RN [1]  
RP SEQUENCE FROM N.A.  
RC TISSUE=Brain;  
RA Coulson E.J., Paliga K., Beyreuther K., Masters C.L.;  
RT "What the evolution of the amyloid protein precursor supergene family  
RT tells us about its function.";  
RL Neurochem. Int. 0:0-0(2000).  
DR EMBL; AF030341; AAF12698.1; -.  
DR HSSP; P05067; 1BA4.  
DR GO; GO:0016020; C:membrane; IEA.  
DR InterPro; IPR008155; A4\_APP.  
DR InterPro; IPR008154; A4\_extra.  
DR InterPro; IPR001255; Beta-APP.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR Pfam; PF03494; Beta-APP; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
FT NON\_TER 1 1  
SQ SEQUENCE 569 AA; 64753 MW; 0AB8BB851863A19D CRC64;

Query Match 100.0%; Score 217; DB 13; Length 569;  
Best Local Similarity 100.0%; Pred. No. 7.5e-20;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||  
 Db 472 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 513

RESULT 7

Q9DGJ8

ID Q9DGJ8 PRELIMINARY; PRT; 695 AA.  
 AC Q9DGJ8;  
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)  
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Beta-amyloid precursor protein 695 isoform.  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Sarasa M., Rodolosse A., Sorribas V.;  
 RT "Cloning of full-length chicken beta-amyloid precursor protein  
 RT isoforms.";  
 RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.  
 DR EMBL; AF289218; AAG00593.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 SQ SEQUENCE 695 AA; 78565 MW; F201ED02AEC86D95 CRC64;

Query Match 100.0%; Score 217; DB 13; Length 695;  
 Best Local Similarity 100.0%; Pred. No. 9.3e-20;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||  
 Db 597 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 638

RESULT 8

Q9DGJ7

ID Q9DGJ7 PRELIMINARY; PRT; 751 AA.  
 AC Q9DGJ7;  
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)  
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Beta-amyloid precursor protein 751 isoform.  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Sarasa M., Rodolosse A., Sorribas V.;  
 RT "Cloning of full-length chicken beta-amyloid precursor protein  
 RT isoforms.";  
 RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.  
 DR EMBL; AF289219; AAG00594.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Protease inhibitor; Serine protease inhibitor.  
 SQ SEQUENCE 751 AA; 84705 MW; E78E9413A8033D84 CRC64;

Query Match 100.0%; Score 217; DB 13; Length 751;  
 Best Local Similarity 100.0%; Pred. No. 1e-19;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||  
 Db 653 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 694

# RESULT 9

O35463

ID O35463 PRELIMINARY; PRT; 79 AA.  
 AC O35463;  
 DT 01-JAN-1998 (TrEMBLrel. 05, Created)  
 DT 01-JAN-1998 (TrEMBLrel. 05, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Alzheimer's amyloid beta protein (Fragment).  
 GN BETA APP.  
 OS Cricetulus griseus (Chinese hamster).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae;  
 OC Cricetulus.  
 OX NCBI\_TaxID=10029;  
 RN [1]  
 RP SEQUENCE FROM N.A.



Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
|||||:|||||||  
Db 120 DAEFGHDSGFEVRHOKLVFFAEDVGSNKGAIIGLMVGGVVIA 161

RESULT 11

Q8BPC7

```

ID      Q8BPC7              PRELIMINARY;          PRT;      384 AA.
AC      Q8BPC7;
DT      01-MAR-2003 (TrEMBLrel. 23, Created)
DT      01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT      01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE      Amyloid beta (Fragment).
GN      APP.
OS      Mus musculus (Mouse).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX      NCBI_TaxID=10090;
RN      [1]
RP      SEQUENCE FROM N.A.
RC      STRAIN=C57BL/6J; TISSUE=Head;
RX      MEDLINE=22354683; PubMed=12466851;
RA      The FANTOM Consortium,
RA      the RIKEN Genome Exploration Research Group Phase I & II Team;
RT      "Analysis of the mouse transcriptome based on functional annotation of
RT      60,770 full-length cDNAs.";
RL      Nature 420:563-573(2002).
DR      EMBL; AK076506; BAC36369.1; -.
DR      MGD; MGI:88059; App.
DR      GO; GO:0005515; F:protein binding; IPI.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR001255; Beta-APP.
DR      Pfam; PF03494; Beta-APP; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PROSITE; PS00320; A4_INTRA; 1.
FT      NON_TER      1      1
SQ      SEQUENCE      384 AA; 43990 MW; A81B1AD8AE683173 CRC64;

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Query Match 91.2%; Score 198; DB 11; Length 384;  
Best Local Similarity 92.9%; Pred. No. 1.5e-17;  
Matches 39; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
||||| :|||  
Db 286 DAEFGHDSGFVVRHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 327

RESULT 12

Q98SG0

```

> ID      Q98SG0      PRELIMINARY;      PRT;      693 AA.
> AC      Q98SG0;
> DT      01-JUN-2001 (TrEMBLrel. 17, Created)
> DT      01-JUN-2001 (TrEMBLrel. 17, Last sequence update)
> DT      01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
> DE      Beta-amyloid precursor protein A.
> GN      APP.
> OS      Xenopus laevis (African clawed frog).

```









Search completed: July 15, 2004, 18:03:53  
Job time : 38 secs

OM protein - protein search, using sw model

Run on: July 15, 2004, 18:00:43 ; Search time 13 Seconds  
(without alignments)  
168.227 Million cell updates/sec

Title: US-09-724-940-42  
Perfect score: 217  
Sequence: 1 DAEFRHDSGYEVHHQKLVFF.....DVGSNKGAIIGLMVGGVVIA 42

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : SwissProt\_42:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

# SUMMARIES

Result No.	Score	% Query		DB	ID	Description
		Match	Length			
1	217	100.0	57	1	A4_URSMA	Q29149 ursus marit
2	217	100.0	58	1	A4_CANFA	Q28280 canis famil
3	217	100.0	58	1	A4_RABIT	Q28748 oryctolagus
4	217	100.0	58	1	A4_SHEEP	Q28757 ovis aries
5	217	100.0	59	1	A4_BOVIN	Q28053 bos taurus
6	217	100.0	751	1	A4_SAIISC	Q95241 s amyloid b
7	217	100.0	770	1	A4_CAVPO	Q60495 c amyloid b
8	217	100.0	770	1	A4_HUMAN	P05067 h amyloid b
9	217	100.0	770	1	A4_MACFA	P53601 m amyloid b
10	217	100.0	770	1	A4_PIG	P79307 s amyloid b
11	198	91.2	770	1	A4_MOUSE	P12023 m amyloid b
12	198	91.2	770	1	A4_RAT	P08592 r amyloid b
13	175	80.6	780	1	A4_TETFL	O73683 tetraodon f
14	171	78.8	737	1	A4_FUGRU	O93279 fugu rubrip
15	62	28.6	755	1	TR2M_AGR4	P04029 agrobacteri
16	61	28.1	755	1	TR2N_AGRVI	P25017 agrobacteri
17	57	26.3	327	1	POLG_PVYCH	P21294 potato viru

18	57	26.3	503	1	Y226_MYCPN	P75462	mycoplasma
19	56.5	26.0	378	1	SLG1_YEAST	P54867	saccharomyc
20	55.5	25.6	251	1	TPIS_XANCP	Q8p7t0	xanthomonas
21	55.5	25.6	297	1	FTR_ARCFU	O28076	archaeoglob
22	55	25.3	488	1	DHAL_PSESP	P33008	pseudomonas
23	55	25.3	3063	1	POLG_PVYN	P18247	p genome po
24	54.5	25.1	967	1	PDB1_ARATH	P93733	arabidopsis
25	54	24.9	239	1	PYRH_CHLTE	P59003	chlorobium
26	54	24.9	284	1	POLG_PVYYO	P11897	potato viru
27	53.5	24.7	251	1	TPIS_XANAC	Q8pj38	xanthomonas
28	53.5	24.7	708	1	YNZB_CAEEL	P45972	caenorhabdi
29	53.5	24.7	971	1	Y228_BORBU	O51246	borrelia bu
30	53	24.4	685	1	HPPA_NITEU	Q82tf3	nitrosomona
31	52	24.0	611	1	YCR3_YEAST	P25351	saccharomyc
32	51	23.5	282	1	UPK_CHLTE	Q8kfj7	chlorobium
33	51	23.5	494	1	COBQ_MYCTU	O53677	mycobacteri
34	51	23.5	769	1	ITB2_BOVIN	P32592	bos taurus
35	50.5	23.3	245	1	Y191_LISMO	Q8yae0	listeria mo
36	50.5	23.3	245	1	Y230_LISIN	Q92f76	listeria in
37	50.5	23.3	915	1	PDB2_ARATH	O23078	arabidopsis
38	50.5	23.3	1150	1	S126_HUMAN	Q9uhw9	homo sapien
39	50.5	23.3	1150	1	S126_MOUSE	Q924n4	mus musculu
40	50	23.0	285	1	MENB_HAEIN	P44960	haemophilus
41	50	23.0	1046	1	IF2_STRAW	Q82k53	streptomyce
42	50	23.0	1437	1	MRP5_HUMAN	O15440	homo sapien
43	50	23.0	3579	1	STAN_DROME	Q9v5n8	drosophila
44	49.5	22.8	1162	1	VGL2_IBVM	P12651	avian infec
45	49	22.6	246	1	TPIS_CULTA	P30741	culex tarsa

# ALIGNMENTS

## RESULT 1

### A4\_URSMA

ID A4\_URSMA STANDARD; PRT; 57 AA.  
AC Q29149;  
DT 01-NOV-1997 (Rel. 35, Created)  
DT 01-NOV-1997 (Rel. 35, Last sequence update)  
DT 30-MAY-2000 (Rel. 39, Last annotation update)  
DE Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid  
DE protein (Beta-APP) (A-beta)] (Fragment).  
GN APP.  
OS Ursus maritimus (Polar bear) (Thalarctos maritimus).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Carnivora; Fissipedia; Ursidae; Ursus.  
OX NCBI\_TaxID=29073;  
RN [1]  
RP SEQUENCE FROM N.A.  
RC TISSUE=Brain;  
RX MEDLINE=92017079; PubMed=1656157;  
RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;  
RT "Conservation of the sequence of the Alzheimer's disease amyloid  
RT peptide in dog, polar bear and five other mammals by cross-species  
RT polymerase chain reaction analysis."  
RL Brain Res. Mol. Brain Res. 10:299-305(1991).  
CC -!- FUNCTION: Functional neuronal receptor which couples to

```

CC      intracellular signaling pathway through the GTP-binding protein
CC      G(O) (By similarity).
CC      -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC      -!- SIMILARITY: Belongs to the APP family.

```

```

DR      EMBL; X56128; CAA39593.1; -.
DR      PIR; B60045; B60045.
DR      HSSP; P05067; 1BA4.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR001255; Beta-APP.
DR      Pfam; PF03494; Beta-APP; 1.
DR      PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR      PROSITE; PS00320; A4_INTRA; PARTIAL.
KW      Glycoprotein; Amyloid; Neurone; Transmembrane.
FT      NON_TER      1      1
FT      CHAIN      6      48      BETA-AMYLOID PROTEIN (POTENTIAL).
FT      DOMAIN      <1      33      EXTRACELLULAR (POTENTIAL).
FT      TRANSMEM      34      57      POTENTIAL.
FT      NON_TER      57      57
SQ      SEQUENCE      57 AA;      6172 MW;      84209D88EBA82DFA CRC64;

```

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
| | | | | | | | | | | | | | | | | | | | | |  
Db 6 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 47







OS Ovis aries (Sheep).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;  
 OC Bovidae; Caprinae; Ovis.  
 OX NCBI\_TaxID=9940;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Heart;  
 RX MEDLINE=92017079; PubMed=1656157;  
 RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;  
 RT "Conservation of the sequence of the Alzheimer's disease amyloid  
 RT peptide in dog, polar bear and five other mammals by cross-species  
 RT polymerase chain reaction analysis."  
 RL Brain Res. Mol. Brain Res. 10:299-305(1991).  
 CC -!- FUNCTION: Functional neuronal receptor which couples to  
 CC intracellular signaling pathway through the GTP-binding protein  
 CC G(O) (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
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 CC use by non-profit institutions as long as its content is in no way  
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 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----  
 DR EMBL; X56130; CAA39595.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; PARTIAL.  
 DR PROSITE; PS00320; A4\_INTRA; PARTIAL.  
 KW Glycoprotein; Amyloid; Neurone; Transmembrane.  
 FT NON\_TER 1 1  
 FT CHAIN 6 48 BETA-AMYLOID PROTEIN (POTENTIAL).  
 FT DOMAIN <1 33 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 34 57 POTENTIAL.  
 FT DOMAIN 58 >58 CYTOPLASMIC (POTENTIAL).  
 FT NON\_TER 58 58  
 SQ SEQUENCE 58 AA; 6300 MW; F434209D88EBA82D CRC64;

Query Match 100.0%; Score 217; DB 1; Length 58;  
 Best Local Similarity 100.0%; Pred. No. 7.6e-22;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||||  
 Db 6 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 47

RESULT 5  
 A4\_BOVIN  
 ID A4\_BOVIN STANDARD; PRT; 59 AA.  
 AC Q28053;

DT 01-NOV-1997 (Rel. 35, Created)  
 DT 01-NOV-1997 (Rel. 35, Last sequence update)  
 DT 30-MAY-2000 (Rel. 39, Last annotation update)  
 DE Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid  
 DE protein (Beta-APP) (A-beta)] (Fragment).  
 GN APP.  
 OS Bos taurus (Bovine).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;  
 OC Bovidae; Bovinae; Bos.  
 OX NCBI\_TaxID=9913;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Brain;  
 RX MEDLINE=92017079; PubMed=1656157;  
 RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;  
 RT "Conservation of the sequence of the Alzheimer's disease amyloid  
 RT peptide in dog, polar bear and five other mammals by cross-species  
 RT polymerase chain reaction analysis."  
 RL Brain Res. Mol. Brain Res. 10:299-305(1991).  
 CC -!- FUNCTION: Functional neuronal receptor which couples to  
 CC intracellular signaling pathway through the GTP-binding protein  
 CC G(O) (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -----  
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 CC use by non-profit institutions as long as its content is in no way  
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 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----  
 DR EMBL; X56124; CAA39589.1; -.  
 DR EMBL; X56126; CAA39591.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; PARTIAL.  
 DR PROSITE; PS00320; A4\_INTRA; PARTIAL.  
 KW Glycoprotein; Amyloid; Neurone; Transmembrane.  
 FT NON\_TER 1 1  
 FT CHAIN 7 49 BETA-AMYLOID PROTEIN (POTENTIAL).  
 FT DOMAIN <1 34 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 35 58 POTENTIAL.  
 FT DOMAIN 59 >59 CYTOPLASMIC (POTENTIAL).  
 FT NON\_TER 59 59  
 SQ SEQUENCE 59 AA; 6414 MW; F43469D488A2E12D CRC64;  
  
 Query Match 100.0%; Score 217; DB 1; Length 59;  
 Best Local Similarity 100.0%; Pred. No. 7.8e-22;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
  
 Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 ||||||||||||||||||||||||||||||||||||

## RESULT 6

## A4\_SAISC

ID A4\_SAISC STANDARD; PRT; 751 AA.  
AC Q95241;  
DT 15-DEC-1998 (Rel. 37, Created)  
DT 15-DEC-1998 (Rel. 37, Last sequence update)  
DT 10-OCT-2003 (Rel. 42, Last annotation update)  
DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid  
DE protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble  
DE APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);  
DE Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-  
DE CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)  
DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-  
DE secretase C-terminal fragment 50); C31].  
GN APP.  
OS Saimiri sciureus (Common squirrel monkey).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.  
OX NCBI\_TaxID=9521;  
RN [1]  
RP SEQUENCE FROM N.A.  
RC TISSUE=Kidney, and Liver;  
RX MEDLINE=96108492; PubMed=8532114;  
RA Levy E., Amorim A., Frangione B., Walker L.C.;  
RT "Beta-amyloid precursor protein gene in squirrel monkeys with  
RT cerebral amyloid angiopathy."  
RL Neurobiol. Aging 16:805-808(1995).  
CC -!- FUNCTION: Functions as a cell surface receptor and performs  
CC physiological functions on the surface of neurons relevant to  
CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
CC cell mobility and transcription regulation through protein-protein  
CC interactions (By similarity). Can promote transcription activation  
CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
CC interaction with Numb (By similarity). Couples to apoptosis-  
CC inducing pathways such as those mediated by G(O) and JIP (By  
CC similarity). Inhibits G(O) alpha ATPase activity (By similarity).  
CC Acts as a kinesin I membrane receptor, mediating the axonal  
CC transport of beta-secretase and presenilin 1 (By similarity). May  
CC be involved in copper homeostasis/oxidative stress through copper  
CC ion reduction. In vitro, copper-metallated APP induces neuronal  
CC death directly or is potentiated through Cu(II)-mediated low-  
CC density lipoprotein oxidation (By similarity). Can regulate  
CC neurite outgrowth through binding to components of the  
CC extracellular matrix such as heparin and collagen I and IV (By  
CC similarity). The splice isoforms that contain the BPTI domain  
CC possess protease inhibitor activity (By similarity).  
CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
CC with metal-reducing activity. Bind transient metals such as  
CC copper, zinc and iron (By similarity).  
CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
CC peptides, including C31, are potent enhancers of neuronal  
CC apoptosis (By similarity).  
CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
CC cytoplasmic proteins, including APBB family members, the APBA

family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding to Dab1 inhibits its serine phosphorylation (By similarity). Also interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1. In vitro, it binds MAPT via the MT-binding domains (By similarity). Associates with microtubules in the presence of ATP and in a kinesin-dependent manner (By similarity).

-!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface protein that rapidly becomes internalized via clathrin-coated pits. During maturation, the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes. Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface. Gamma-CTF(59) peptide is located to both the cytoplasm and nuclei of neurons (By similarity).

-!- ALTERNATIVE PRODUCTS:  
 Event=Alternative splicing; Named isoforms=2;  
 Comment=Additional isoforms seem to exist;  
 Name=APP770;  
 IsoId=Q95241-1; Sequence=Displayed;  
 Name=APP695;  
 IsoId=Q95241-2; Sequence=Not described;

-!- DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells (By similarity).

-!- DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue. The NPXY site is also involved in clathrin-mediated endocytosis (By similarity).

-!- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the retention of corresponding membrane-anchored C-terminal fragments, C83 and C99. Subsequent processing of C83 by gamma-secretase yields P3 peptides. This is the major secretory pathway and is nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated gamma-secretase processing of C99 releases the amyloid beta proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42), major components of amyloid plaques, and the cytotoxic C-terminal fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By similarity).

-!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9 results in the production of the neurotoxic C31 peptide and the increased production of beta-amyloid peptides (By similarity).

-!- PTM: N- and O-glycosylated (By similarity).

-!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and serine residues is neuron-specific. Phosphorylation can affect APP

CC processing, neuronal differentiation and interaction with other  
 CC proteins (By similarity).  
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC resulting in beta-amyloid-metal aggregates (By similarity).  
 CC Extracellular zinc-binding increases binding of heparin to APP and  
 CC inhibits collagen-binding (By similarity).  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
 CC -----  
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 CC -----  
 DR EMBL; S81024; AAD14347.1; -.  
 DR HSSP; P05067; 1AAP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Amyloid; Alternative splicing.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 751 A4 PROTEIN.  
 FT CHAIN 18 668 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 652 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 653 751 C99 (POTENTIAL).  
 FT CHAIN 653 694 BETA-AMYLOID PROTEIN 42 (POTENTIAL).  
 FT CHAIN 653 692 BETA-AMYLOID PROTEIN 40 (POTENTIAL).  
 FT CHAIN 669 751 C83 (POTENTIAL).  
 FT CHAIN 669 694 P3(42) (POTENTIAL).  
 FT CHAIN 669 692 P3(40) (POTENTIAL).  
 FT CHAIN 693 751 GAMMA-CTF(59) (POTENTIAL).  
 FT CHAIN 695 751 GAMMA-CTF(57) (POTENTIAL).  
 FT CHAIN 702 751 GAMMA-CTF(50) (POTENTIAL).  
 FT CHAIN 721 751 C31 (POTENTIAL).  
 FT DOMAIN 18 680 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 681 704 POTENTIAL.  
 FT DOMAIN 705 751 CYTOPLASMIC (POTENTIAL).

FT	DOMAIN	96	110	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	181	188	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	291	341	BPTI/KUNITZ INHIBITOR.
FT	DOMAIN	316	344	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	363	428	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	504	521	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	713	732	INTERACTION WITH G(O)-ALPHA
FT				(BY SIMILARITY).
FT	DOMAIN	230	260	ASP/GLU-RICH (ACIDIC).
FT	DOMAIN	274	280	POLY-THR.
FT	SITE	144	144	REQUIRED FOR COPPER(II) REDUCTION
FT				(BY SIMILARITY).
FT	ACT_SITE	301	302	REACTIVE BOND.
FT	SITE	652	653	CLEAVAGE (BY BETA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	653	654	CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT	SITE	668	669	CLEAVAGE (BY ALPHA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	685	685	INVOLVED IN FREE RADICAL PROPAGATION
FT				(BY SIMILARITY).
FT	SITE	687	687	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	692	693	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	694	695	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	701	702	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT				(BY SIMILARITY).
FT	SITE	705	715	BASOLATERAL SORTING SIGNAL
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)
FT				(BY SIMILARITY).
FT	SITE	738	741	ENDOCYTOSIS SIGNAL.
FT	SITE	740	743	NPXY MOTIF.

Query Match 100.0%; Score 217; DB 1; Length 751;  
 Best Local Similarity 100.0%; Pred. No. 9.6e-21;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||  
 Db 653 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 694

# RESULT 7

A4\_CAVPO

ID A4\_CAVPO STANDARD; PRT; 770 AA.  
 AC Q60495; Q60496;  
 DT 10-OCT-2003 (Rel. 42, Created)  
 DT 10-OCT-2003 (Rel. 42, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease  
 DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);  
 DE Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid  
 DE protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);  
 DE P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-  
 DE CTF(57) (Gamma-secretase C-terminal fragment 57); C31].

GN APP.  
 OS *Cavia porcellus* (Guinea pig).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; *Cavia*.  
 OX NCBI\_TaxID=10141;  
 RN [1]  
 RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.  
 RC TISSUE=Brain, and Liver;  
 RX MEDLINE=97236426; PubMed=9116031;  
 RA Beck M., Mueller D., Bigl V.;  
 RT "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and  
 RT alternative splicing.";  
 RL Biochim. Biophys. Acta 1351:17-21(1997).  
 RN [2]  
 RP INTERACTION OF BETA-APP40 WITH APOE.  
 RX MEDLINE=98007700; PubMed=9349544;  
 RA Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,  
 RA Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;  
 RT "Isoform-specific effects of apolipoproteins E2, E3, and E4 on  
 RT cerebral capillary sequestration and blood-brain barrier transport of  
 RT circulating Alzheimer's amyloid beta.";  
 RL J. Neurochem. 69:1995-2004(1997).  
 RN [3]  
 RP PROCESSING.  
 RX MEDLINE=20084499; PubMed=10619481;  
 RA Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,  
 RA Bigl V.;  
 RT "Guinea-pig primary cell cultures provide a model to study expression  
 RT and amyloidogenic processing of endogenous amyloid precursor  
 RT protein.";  
 RL Neuroscience 95:243-254(2000).  
 RN [4]  
 RP GAMMA-SECRETASE PROCESSING.  
 RX MEDLINE=20576391; PubMed=11035007;  
 RA Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,  
 RA Ziani-Cherif C., Onstead L., Sambamurti K.;  
 RT "A novel gamma -secretase assay based on detection of the putative  
 RT C-terminal fragment-gamma of amyloid beta protein precursor.";  
 RL J. Biol. Chem. 276:481-487(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(0) and JIP (By  
 CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).  
 CC Acts as a kinesin I membrane receptor, mediating the axonal  
 CC transport of beta-secretase and presenilin 1 (By similarity). May  
 CC be involved in copper homeostasis/oxidative stress through copper  
 CC ion reduction (By similarity). In vitro, copper-metallated APP  
 CC induces neuronal death directly or is potentiated through Cu(II)-  
 CC mediated low-density lipoprotein oxidation (By similarity). Can  
 CC regulate neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity). The splice isoforms that contain the BPTI domain

possess protease inhibitor activity (By similarity).

CC    -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC    with metal-reducing activity. Bind transient metals such as  
 CC    copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins  
 CC    and apolipoproteins E and J in the CSF and to HDL particles in  
 CC    plasma, inhibiting metal-catalyzed oxidation of lipoproteins.

CC    -!- FUNCTION: Appicans elicit adhesion of neural cells to the  
 CC    extracellular matrix and may regulate neurite outgrowth in the  
 CC    brain (By similarity).

CC    -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC    peptides, including C31, are potent enhancers of neuronal  
 CC    apoptosis (By similarity).

CC    -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC    cytoplasmic proteins, including APBB family members, the APBA  
 CC    family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also  
 CC    interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC    (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity).  
 CC    Associates with microtubules in the presence of ATP and in a  
 CC    kinesin-dependent manner (By similarity). Soluble Abeta40 binds  
 CC    all three isoforms of APOE, in vitro and in vivo. When lipidated,  
 CC    ApoE3 appears to be the preferred amyloid binding isoform, while  
 CC    the apoE4 isoform-beta-APP40 complex is capable of being  
 CC    transported across the blood-brain barrier.

CC    -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC    protein that rapidly becomes internalized via clathrin-coated pits  
 CC    (By similarity). During maturation, the immature APP (N-  
 CC    glycosylated in the endoplasmic reticulum) moves to the Golgi  
 CC    complex where complete maturation occurs (O-glycosylated and  
 CC    sulfated) (By similarity). After alpha-secretase cleavage, soluble  
 CC    APP is released into the extracellular space and the C-terminal is  
 CC    internalized to endosomes and lysosomes (By similarity). Some APP  
 CC    accumulates in secretory transport vesicles leaving the late Golgi  
 CC    compartment and returns to the cell surface (By similarity). APP  
 CC    sorts to the basolateral surface in epithelial cells (By  
 CC    similarity).

CC    -!- ALTERNATIVE PRODUCTS:  
 CC    Event=Alternative splicing; Named isoforms=2;  
 CC    Comment=Additional isoforms, missing exons 7,8 and 15, seem to  
 CC    exist. The L-isoforms, missing exon 15, are referred to as  
 CC    appicans;  
 CC    Name=APP770;  
 CC    IsoId=Q60495-1; Sequence=Displayed;  
 CC    Name=APP695;  
 CC    IsoId=Q60495-2; Sequence=VSP\_007221, VSP\_007222;

CC    -!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in  
 CC    brain. The longer isoforms containing the BPTI domain are  
 CC    predominantly expressed in peripheral organs such as muscle and  
 CC    liver.

CC    -!- INDUCTION: Increased levels during neuronal differentiation.

CC    -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC    sorting of membrane proteins to the basolateral surface of  
 CC    epithelial cells.

CC    -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC    phosphorylated proteins is required for the specific binding of  
 CC    the PID domain. However additional amino acids either N- or C-  
 CC    terminal to the NPXY motif are often required for complete  
 CC    interaction. The PID domain-containing proteins which bind APP



require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue (By similarity). The NPXY site is also involved in clathrin-mediated endocytosis.

- !- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the retention of corresponding membrane-anchored C-terminal fragments, CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by gamma-secretase yields P3 peptides. This is the major secretory pathway and is nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated gamma-secretase processing of CTF-beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42), major components of amyloid plaques, and the corresponding cytotoxic C-terminal fragments (CTFs).
- !- PTM: Proteolytically cleaved by caspase-3 during neuronal apoptosis (By similarity).
- !- PTM: N- and O-glycosylated. O-linkage of chondroitin sulfate to the L-APP isoforms produces the APP proteoglycan core proteins, the appicans (By similarity).
- !- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and serine residues is neuron-specific (By similarity). Phosphorylation can affect APP processing, neuronal differentiation and interaction with other proteins.
- !- PTM: Extracellular binding and reduction of copper, results in a corresponding oxidation of Cys-144 and Cys-158, and the formation of a disulfide bond (By similarity).
- !- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and zinc, can induce histidine-bridging between beta-amyloid molecules resulting in beta-amyloid-metal aggregates.
- !- SIMILARITY: Belongs to the APP family.
- !- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

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EMBL; X97631; CAA66230.1; -.  
 EMBL; X99198; CAA67589.1; -.  
 HSSP; P05067; 1BA4.  
 InterPro; IPR008155; A4\_APP.  
 InterPro; IPR008154; A4\_extra.  
 InterPro; IPR002223; Kunitz\_BPTI.  
 Pfam; PF00014; Kunitz\_BPTI; 1.  
 PRINTS; PR00203; AMYLOIDA4.  
 PRINTS; PR00759; BASICPTASE.  
 ProDom; PD000222; Kunitz\_BPTI; 1.  
 SMART; SM00006; A4\_EXTRA; 1.  
 SMART; SM00131; KU; 1.  
 PROSITE; PS00319; A4\_EXTRA; 1.  
 PROSITE; PS00320; A4\_INTRA; 1.

DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Alternative splicing; Amyloid.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.  
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (BY SIMILARITY).  
 FT CHAIN 18 671 SOLUBLE APP-BETA (BY SIMILARITY).  
 FT CHAIN 672 770 CTF-ALPHA (BY SIMILARITY).  
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).  
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).  
 FT CHAIN 688 770 CTF-BETA (BY SIMILARITY).  
 FT CHAIN 688 713 P3(42) (BY SIMILARITY).  
 FT CHAIN 688 711 P3(40) (BY SIMILARITY).  
 FT CHAIN 712 770 GAMMA-CTF(59) (BY SIMILARITY).  
 FT CHAIN 714 770 GAMMA-CTF(57) (BY SIMILARITY).  
 Query Match 100.0%; Score 217; DB 1; Length 770;  
 Best Local Similarity 100.0%; Pred. No. 9.9e-21;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||  
 Db 672 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 713

# RESULT 8

## A4\_HUMAN

ID A4\_HUMAN STANDARD; PRT; 770 AA.  
 AC P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q16014;  
 AC Q16019; Q16020; Q9BT38; Q9UCA9; Q9UCB6; Q9UCC8; Q9UCD1; Q9UQ58;  
 DT 13-AUG-1987 (Rel. 05, Created)  
 DT 01-NOV-1991 (Rel. 20, Last sequence update)  
 DT 15-MAR-2004 (Rel. 43, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease  
 DE amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease  
 DE nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-  
 DE alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42  
 DE (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);  
 DE P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)  
 DE (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-  
 DE secretase C-terminal fragment 57) (Amyloid intracellular domain 57)  
 DE (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)  
 DE (Amyloid intracellular domain 50) (AID(50)); C31].  
 GN APP OR A4 OR AD1.  
 OS Homo sapiens (Human).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.  
 OX NCBI\_TaxID=9606;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=87144572; PubMed=2881207;  
 RA Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,  
 RA Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;

RT "The precursor of Alzheimer's disease amyloid A4 protein resembles a  
 RT cell-surface receptor."  
 RL Nature 325:733-736(1987).  
 RN [2]  
 RP SEQUENCE FROM N.A. (ISOFORM APP751).  
 RC TISSUE=Brain;  
 RX MEDLINE=88122639; PubMed=2893289;  
 RA Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,  
 RA Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,  
 RA Cordell B.;  
 RT "A new A4 amyloid mRNA contains a domain homologous to serine  
 RT proteinase inhibitors."  
 RL Nature 331:525-527(1988).  
 RN [3]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RX MEDLINE=89128427; PubMed=2783775;  
 RA Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,  
 RA Unterbeck A., Beyreuther K., Mueller-Hill B.;  
 RT "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid  
 RT is encoded by 16 exons."  
 RL Nucleic Acids Res. 17:517-522(1989).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM APP770).  
 RX MEDLINE=90236318; PubMed=2110105;  
 RA Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;  
 RT "Genomic organization of the human amyloid beta-protein precursor  
 RT gene."  
 RL Gene 87:257-263(1990).  
 RN [5]  
 RP ERRATUM, AND REVISIONS.  
 RA Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;  
 RL Gene 102:291-292(1991).  
 RN [6]  
 RP SEQUENCE FROM N.A. (ISOFORM L-APP733).  
 RC TISSUE=Leukocyte;  
 RX MEDLINE=92268136; PubMed=1587857;  
 RA Koenig G., Moenning U., Czech C., Prior R., Banati R.,  
 RA Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;  
 RT "Identification and differential expression of a novel alternative  
 RT splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in  
 RT leukocytes and brain microglial cells."  
 RL J. Biol. Chem. 267:10804-10809(1992).  
 RN [7]  
 RP SEQUENCE FROM N.A. (ISOFORM APP770).  
 RX MEDLINE=97263807; PubMed=9108164;  
 RA Hattori M., Tsukahara F., Furuhashi Y., Tanahashi H., Hirose M.,  
 RA Saito M., Tsukuni S., Sakaki Y.;  
 RT "A novel method for making nested deletions and its application for  
 RT sequencing of a 300 kb region of human APP locus."  
 RL Nucleic Acids Res. 25:1802-1808(1997).  
 RN [8]  
 RP SEQUENCE FROM N.A. (ISOFORM APP639).  
 RC TISSUE=Brain;  
 RX MEDLINE=22744650; PubMed=12859342;  
 RA Tang K., Wang C., Shen C., Sheng S., Ravid R., Jing N.;  
 RT "Identification of a novel alternative splicing isoform of human  
 RT amyloid precursor protein gene, APP639."

RL Eur. J. Neurosci. 18:102-108(2003).  
 RN [9]  
 RP SEQUENCE FROM N.A. (ISOFORM APP305).  
 RC TISSUE=Pancreas;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [10]  
 RP SEQUENCE OF 1-10 FROM N.A.  
 RC TISSUE=Liver;  
 RX MEDLINE=89016647; PubMed=3140222;  
 RA Schon E.A., Mita S., Sadlock J., Herbert J.;  
 RT "A cDNA specifying the human amyloid beta precursor protein (ABPP)  
 RT encodes a 95-kDa polypeptide.";  
 RL Nucleic Acids Res. 16:9351-9351(1988).  
 RN [11]  
 RP ERRATUM, AND REVISIONS.  
 RA Mita S., Sadlock J., Herbert J., Schon E.A.;  
 RL Nucleic Acids Res. 16:11402-11402(1988).  
 RN [12]  
 RP SEQUENCE OF 1-75 FROM N.A.  
 RX MEDLINE=89165870; PubMed=2538123;  
 RA La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;  
 RT "Characterization of the 5'-end region and the first two exons of the  
 RT beta-protein precursor gene.";  
 RL Biochem. Biophys. Res. Commun. 159:297-304(1989).  
 RN [13]  
 RP SEQUENCE OF 18-50.  
 RC TISSUE=Fibroblast;  
 RX MEDLINE=87250462; PubMed=3597385;  
 RA van Nostrand W.E., Cunningham D.D.;  
 RT "Purification of protease nexin II from human fibroblasts.";  
 RL J. Biol. Chem. 262:8508-8514(1987).  
 RN [14]  
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).  
 RC TISSUE=Brain;  
 RX MEDLINE=89346754; PubMed=2569763;  
 RA de Sauvage F., Octave J.N.;  
 RT "A novel mRNA of the A4 amyloid precursor gene coding for a possibly

RT secreted protein.";  
 RL Science 245:651-653(1989).  
 RN [15]  
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=87231971; PubMed=3035574;  
 RA Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;  
 RT "Molecular cloning and characterization of a cDNA encoding the  
 RT cerebrovascular and the neuritic plaque amyloid peptides.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).  
 RN [16]  
 RP SEQUENCE OF 286-366 FROM N.A.  
 RX MEDLINE=88122640; PubMed=2893290;  
 RA Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,  
 RA Gusella J.F., Neve R.L.;  
 RT "Protease inhibitor domain encoded by an amyloid protein precursor  
 RT mRNA associated with Alzheimer's disease.";  
 RL Nature 331:528-530(1988).  
 RN [17]  
 RP SEQUENCE OF 287-367 FROM N.A.  
 RX MEDLINE=88122641; PubMed=2893291;  
 RA Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;  
 RT "Novel precursor of Alzheimer's disease amyloid protein shows  
 RT protease inhibitory activity.";  
 RL Nature 331:530-532(1988).  
 RN [18]  
 RP SEQUENCE OF 507-770 FROM N.A.  
 RC TISSUE=Brain cortex;  
 RX MEDLINE=88124954; PubMed=2893379;  
 RA Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,  
 RA Marotta C.A.;  
 RT "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer  
 RT disease brain: coding and noncoding regions of the fetal precursor  
 RT mRNA are expressed in the cortex.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).  
 RN [19]  
 RP SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.  
 RX MEDLINE=96139497; PubMed=8576160;  
 RA Beher D., Hesse L., Masters C.L., Multhaup G.;  
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and  
 RT mapping of the binding sites on APP and collagen type I.";  
 RL J. Biol. Chem. 271:1613-1620(1996).  
 RN [20]  
 RP SEQUENCE OF 655-737 FROM N.A., AND VARIANTS AD PHE-717; AD ILE-717  
 RP AND AD GLY-717.  
 RX MEDLINE=93236601; PubMed=8476439;  
 RA Denman R.B., Rosenzwaig R., Miller D.L.;  
 RT "A system for studying the effect(s) of familial Alzheimer disease  
 RT mutations on the processing of the beta-amyloid peptide precursor.";  
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).  
 RN [21]  
 RP SEQUENCE OF 656-737 FROM N.A.  
 RX MEDLINE=89392030; PubMed=2675837;  
 RA Johnstone E.M., Chaney M.O., Moore R.E., Ward K.E., Norris F.H.,  
 RA Little S.P.;  
 RT "Alzheimer's disease amyloid peptide is encoded by two exons and shows  
 RT similarity to soybean trypsin inhibitor.";

RL Biochem. Biophys. Res. Commun. 163:1248-1255(1989).  
RN [22]

Query Match 100.0%; Score 217; DB 1; Length 770;  
Best Local Similarity 100.0%; Pred. No. 9.9e-21;  
Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
||||||||||||||||||||||||||||||||||||||  
Db 672 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 713

#### RESULT 9

##### A4\_MACFA

ID A4\_MACFA STANDARD; PRT; 770 AA.  
AC P53601; Q95KN7;  
DT 01-OCT-1996 (Rel. 34, Created)  
DT 28-FEB-2003 (Rel. 41, Last sequence update)  
DT 28-FEB-2003 (Rel. 41, Last annotation update)  
DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease  
DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);  
DE Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-  
DE APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);  
DE Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)  
DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-  
DE secretase C-terminal fragment 50); C31].  
GN APP.  
OS Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;  
OC Cercopithecinae; Macaca.  
OX NCBI\_TaxID=9541;  
RN [1]  
RP SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).  
RC TISSUE=Cerebellum;  
RX MEDLINE=91273117; PubMed=1905108;  
RA Podlisny M.B., Tolan D.R., Selkoe D.J.;  
RT "Homology of the amyloid beta protein precursor in monkey and human  
RT supports a primate model for beta amyloidosis in Alzheimer's  
RT disease.";  
RL Am. J. Pathol. 138:1423-1435(1991).  
CC -!- FUNCTION: Functions as a cell surface receptor and performs  
CC physiological functions on the surface of neurons relevant to  
CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
CC cell mobility and transcription regulation through protein-protein  
CC interactions (By similarity). Can promote transcription activation  
CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
CC interaction with Numb (By similarity). Couples to apoptosis-  
CC inducing pathways such as those mediated by G(0) and JIP (By  
CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).  
CC Acts as a kinesin I membrane receptor, mediating the axonal  
CC transport of beta-secretase and presenilin 1 (By similarity). May  
CC be involved in copper homeostasis/oxidative stress through copper  
CC ion reduction. In vitro, copper-metallated APP induces neuronal  
CC death directly or is potentiated through Cu(II)-mediated low-  
CC density lipoprotein oxidation (By similarity). Can regulate  
CC neurite outgrowth through binding to components of the

CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity). The splice isoforms that contain the BPTI domain  
 CC possess protease inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IBL, KNS2  
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete  
 CC maturation occurs (O-glycosylated and sulfated). After alpha-  
 CC secretase cleavage, soluble APP is released into the extracellular  
 CC space and the C-terminal is internalized to endosomes and  
 CC lysosomes. Some APP accumulates in secretory transport vesicles  
 CC leaving the late Golgi compartment and returns to the cell  
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm  
 CC and nuclei of neurons (By similarity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;  
 CC Comment=Additional isoforms seem to exist;  
 CC Name=APP770;  
 CC IsoId=P53601-1; Sequence=Displayed;  
 CC Name=APP695;  
 CC IsoId=P53601-2; Sequence=VSP\_000010, VSP\_000011;  
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC sorting of membrane proteins to the basolateral surface of  
 CC epithelial cells (By similarity).  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The PID domain-containing proteins which bind APP  
 CC require the YENPTY motif for full interaction. These interactions  
 CC are independent of phosphorylation on the terminal tyrosine  
 CC residue. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis (By similarity).  
 CC -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC leads to generation and extracellular release of soluble APP  
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC retention of corresponding membrane-anchored C-terminal fragments,  
 CC C83 and C99. Subsequent processing of C83 by gamma-secretase  
 CC yields P3 peptides. This is the major secretory pathway and is  
 CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
 CC gamma-secretase processing of C99 releases the amyloid beta

CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
 CC major components of amyloid plaques, and the cytotoxic C-terminal  
 CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
 CC similarity).  
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis  
 CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9  
 CC results in the production of the neurotoxic C31 peptide and the  
 CC increased production of beta-amyloid peptides (By similarity).  
 CC -!- PTM: N- and O-glycosylated (By similarity).  
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC serine residues is neuron-specific. Phosphorylation can affect APP  
 CC processing, neuronal differentiation and interaction with other  
 CC proteins (By similarity).  
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC resulting in beta-amyloid-metal aggregates (By similarity).  
 CC Extracellular zinc-binding increases binding of heparin to APP and  
 CC inhibits collagen-binding (By similarity).  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
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 CC use by non-profit institutions as long as its content is in no way  
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 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----  
 DR EMBL; M58727; AAA36829.1; -.  
 DR EMBL; M58726; AAA36828.1; -.  
 DR HSSP; P05067; 1AAP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Alternative splicing; Amyloid.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.  
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 671 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 672 770 C99 (POTENTIAL).



FT	CHAIN	672	713	BETA-AMYLOID PROTEIN 42 (POTENTIAL).
FT	CHAIN	672	711	BETA-AMYLOID PROTEIN 40 (POTENTIAL).
FT	CHAIN	688	770	C83 (POTENTIAL).
FT	CHAIN	688	713	P3(42) (POTENTIAL).
FT	CHAIN	688	711	P3(40) (POTENTIAL).
FT	CHAIN	712	770	GAMMA-CTF(59) (POTENTIAL).
FT	CHAIN	714	770	GAMMA-CTF(57) (POTENTIAL).
FT	CHAIN	721	770	GAMMA-CTF(50) (POTENTIAL).
FT	CHAIN	740	770	C31 (POTENTIAL).
FT	DOMAIN	18	699	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	700	723	POTENTIAL.
FT	DOMAIN	724	770	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	96	110	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	181	188	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	291	341	BPTI/KUNITZ INHIBITOR.
FT	DOMAIN	391	423	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	491	522	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	523	540	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	732	751	INTERACTION WITH G(O)-ALPHA
FT				(BY SIMILARITY).
FT	DOMAIN	230	260	ASP/GLU-RICH (ACIDIC).
FT	DOMAIN	274	280	POLY-THR.
FT	SITE	144	144	REQUIRED FOR COPPER(II) REDUCTION
FT				(BY SIMILARITY).
FT	ACT_SITE	301	302	REACTIVE BOND (BY SIMILARITY).
FT	SITE	671	672	CLEAVAGE (BY BETA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	672	673	CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT	SITE	687	688	CLEAVAGE (BY ALPHA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	704	704	IMPLICATED IN FREE RADICAL PROPAGATION
FT				(BY SIMILARITY).
FT	SITE	706	706	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	711	712	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	713	714	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT				(BY SIMILARITY).
FT	SITE	724	734	BASOLATERAL SORTING SIGNAL
FT				(BY SIMILARITY).
FT	SITE	739	740	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)

Query Match 100.0%; Score 217; DB 1; Length 770;  
 Best Local Similarity 100.0%; Pred. No. 9.9e-21;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||||  
 Db 672 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 713

RESULT 10  
 A4\_PIG  
 ID A4\_PIG STANDARD; PRT; 770 AA.  
 AC P79307; Q29023; Q9TUI0;

DT 01-NOV-1997 (Rel. 35, Created)  
 DT 10-OCT-2003 (Rel. 42, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease  
 DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);  
 DE Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-  
 DE APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);  
 DE Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)  
 DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-  
 DE secretase C-terminal fragment 50); C31].  
 OS *Sus scrofa* (Pig).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; *Sus*.  
 OX NCBI\_TaxID=9823;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Kimura A., Takahashi T.;  
 RT "Amyloid precursor protein 770.";  
 RL Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.  
 RN [2]  
 RP SEQUENCE OF 1-136 FROM N.A.  
 RC TISSUE=Small intestine;  
 RA Winteroe A.K., Fredholm M.;  
 RT "Evaluation and characterization of a porcine small intestine cDNA  
 RT library.";  
 RL Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.  
 RN [3]  
 RP SEQUENCE OF 667-723 FROM N.A.  
 RC TISSUE=Brain;  
 RX MEDLINE=92017079; PubMed=1656157;  
 RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;  
 RT "Conservation of the sequence of the Alzheimer's disease amyloid  
 RT peptide in dog, polar bear and five other mammals by cross-species  
 RT polymerase chain reaction analysis.";  
 RL Brain Res. Mol. Brain Res. 10:299-305(1991).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(0) and JIP (By  
 CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).  
 CC Acts as a kinesin I membrane receptor, mediating the axonal  
 CC transport of beta-secretase and presenilin 1 (By similarity). May  
 CC be involved in copper homeostasis/oxidative stress through copper  
 CC ion reduction (By similarity). In vitro, copper-metallated APP  
 CC induces neuronal death directly or is potentiated through Cu(II)-  
 CC mediated low-density lipoprotein oxidation (By similarity). Can  
 CC regulate neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved

CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IBL, KNS2  
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete  
 CC maturation occurs (O-glycosylated and sulfated). After alpha-  
 CC secretase cleavage, soluble APP is released into the extracellular  
 CC space and the C-terminal is internalized to endosomes and  
 CC lysosomes. Some APP accumulates in secretory transport vesicles  
 CC leaving the late Golgi compartment and returns to the cell  
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm  
 CC and nuclei of neurons (By similarity).  
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC sorting of membrane proteins to the basolateral surface of  
 CC epithelial cells (By similarity).  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The PID domain-containing proteins which bind APP  
 CC require the YENPTY motif for full interaction. These interactions  
 CC are independent of phosphorylation on the terminal tyrosine  
 CC residue. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis (By similarity).  
 CC -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC leads to generation and extracellular release of soluble APP  
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC retention of corresponding membrane-anchored C-terminal fragments,  
 CC C83 and C99. Subsequent processing of C83 by gamma-secretase  
 CC yields P3 peptides. This is the major secretory pathway and is  
 CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
 CC gamma-secretase processing of C99 releases the amyloid beta  
 CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
 CC major components of amyloid plaques, and the cytotoxic C-terminal  
 CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
 CC similarity).  
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis  
 CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9  
 CC results in the production of the neurotoxic C31 peptide and the  
 CC increased production of beta-amyloid peptides (By similarity).  
 CC -!- PTM: N- and O-glycosylated (By similarity).  
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC serine residues is neuron-specific. Phosphorylation can affect APP  
 CC processing, neuronal differentiation and interaction with other  
 CC proteins (By similarity).  
 CC -!- PTM: Extracellular binding and reduction of copper, results in a

CC corresponding oxidation of Cys-144 and Cys-158, and the formation  
 CC of a disulfide bond (By similarity).  
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC resulting in beta-amyloid-metal aggregates (By similarity).  
 CC Extracellular zinc-binding increases binding of heparin to APP and  
 CC inhibits collagen-binding (By similarity).  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
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 CC -----  
 DR EMBL; AB032550; BAA84580.1; -.  
 DR EMBL; Z84022; CAB06313.1; -.  
 DR EMBL; X56127; CAA39592.1; -.  
 DR HSSP; P05067; 1AAP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Amyloid.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.  
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 671 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 672 770 C99 (BY SIMILARITY).  
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).  
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).  
 FT CHAIN 688 770 C83 (BY SIMILARITY).  
 FT CHAIN 688 713 P3(42) (BY SIMILARITY).  
 FT CHAIN 688 711 P3(40) (BY SIMILARITY).  
 FT CHAIN 712 770 GAMMA-CTF(59).  
 FT CHAIN 714 770 GAMMA-CTF(57).  
 FT CHAIN 721 770 GAMMA-CTF(50) (BY SIMILARITY).  
 FT CHAIN 740 770 C31 (DURING APOPTOSIS) (BY SIMILARITY).  
 FT DOMAIN 18 699 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 700 723 POTENTIAL.  
 FT DOMAIN 724 770 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 96 110 HEPARIN-BINDING (BY SIMILARITY).

FT	DOMAIN	135	155	COPPER-BINDING (BY SIMILARITY).
FT	DOMAIN	181	188	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	291	341	BPTI/KUNITZ INHIBITOR.
FT	DOMAIN	391	423	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	491	522	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	523	540	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	732	751	INTERACTION WITH G(O)-ALPHA (BY SIMILARITY).
FT	DOMAIN	230	260	ASP/GLU-RICH (ACIDIC).
FT	DOMAIN	274	280	POLY-THR.
FT	SITE	144	144	REQUIRED FOR COPPER(II) REDUCTION (BY SIMILARITY).
FT	ACT_SITE	301	302	REACTIVE BOND (BY SIMILARITY).
FT	SITE	671	672	CLEAVAGE (BY BETA-SECRETASE) (BY SIMILARITY).
FT	SITE	672	673	CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT	SITE	687	688	CLEAVAGE (BY ALPHA-SECRETASE) (BY SIMILARITY).
FT	SITE	704	704	IMPLICATED IN FREE RADICAL PROPAGATION (BY SIMILARITY).
FT	SITE	706	706	INVOLVED IN OXIDATIVE REACTIONS (BY SIMILARITY).
FT	SITE	711	712	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1) (BY SIMILARITY).
FT	SITE	713	714	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2) (BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)

Query Match 100.0%; Score 217; DB 1; Length 770;  
 Best Local Similarity 100.0%; Pred. No. 9.9e-21;  
 Matches 42; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
 |||||  
 Db 672 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 713

# RESULT 11

## A4\_MOUSE

ID A4\_MOUSE STANDARD; PRT; 770 AA.  
 AC P12023; P97487; P97942; Q99K32;  
 DT 01-OCT-1989 (Rel. 12, Created)  
 DT 10-OCT-2003 (Rel. 42, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease  
 DE amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:  
 DE Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99  
 DE (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein  
 DE 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase  
 DE C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))  
 DE (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)  
 DE (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)  
 DE (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain  
 DE 50) (AID(50)); C31].  
 GN APP.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=88106489; PubMed=3322280;  
 RA Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;  
 RT "Complementary DNA for the mouse homolog of the human amyloid beta  
 RT protein precursor.";  
 RL Biochem. Biophys. Res. Commun. 149:665-671(1987).  
 RN [2]  
 RP REVISIONS.  
 RA Yamada T.;  
 RL Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.  
 RN [3]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC STRAIN=BALB/c; TISSUE=Brain;  
 RX MEDLINE=92096458; PubMed=1756177;  
 RA de Strooper B., van Leuven F., van den Berghe H.;  
 RT "The amyloid beta protein precursor or proteinase nexin II from mouse  
 RT is closer related to its human homolog than previously reported.";  
 RL Biochim. Biophys. Acta 1129:141-143(1991).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC STRAIN=SAMP8; TISSUE=Hippocampus;  
 RX MEDLINE=21130647; PubMed=11235921;  
 RA Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,  
 RA Alvarez J., Morley J.E.;  
 RT "Molecular cloning, expression, and regulation of hippocampal amyloid  
 RT precursor protein of senescence accelerated mouse (SAMP8).";  
 RL Biochem. Cell Biol. 79:57-67(2001).  
 RN [5]  
 RP SEQUENCE OF 1-19 FROM N.A.  
 RX MEDLINE=92209998; PubMed=1555768;  
 RA Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,  
 RA Sakai Y.;  
 RT "Positive and negative regulatory elements for the expression of the  
 RT Alzheimer's disease amyloid precursor-encoding gene in mouse.";  
 RL Gene 112:189-195(1992).  
 RN [6]  
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).  
 RC TISSUE=Breast tumor;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,

RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length human  
 RT and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [7]  
 RP SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.  
 RC TISSUE=Brain, and Kidney;  
 RX MEDLINE=89149813; PubMed=2493250;  
 RA Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;  
 RT "Structure and expression of the alternatively-spliced forms of mRNA  
 RT for the mouse homolog of Alzheimer's disease amyloid beta protein  
 RT precursor.";  
 RL Biochem. Biophys. Res. Commun. 158:906-912(1989).  
 RN [8]  
 RP SEQUENCE OF 289-364 FROM N.A.  
 RC STRAIN=CD-1; TISSUE=Placenta;  
 RX MEDLINE=89345111; PubMed=2569710;  
 RA Fukuchi K., Martin G.M., Deeb S.S.;  
 RT "Sequence of the protease inhibitor domain of the A4 amyloid protein  
 RT precursor of Mus domesticus.";  
 RL Nucleic Acids Res. 17:5396-5396(1989).  
 RN [9]  
 RP SEQUENCE OF 656-737 FROM N.A.  
 RC STRAIN=129/Sv;  
 RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,  
 RA Loring J.F., Goate A.M.;  
 RT "Introduction of six mutations into the mouse genome using 'Hit and  
 RT Run' gene-targeting: introduction of familial Alzheimer's disease  
 RT mutations into the mouse amyloid precursor protein gene and  
 RT humanization of the A-beta fragment.";  
 RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.  
 RN [10]  
 RP TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.  
 RX MEDLINE=93287808; PubMed=8510506;  
 RA Sola C., Mengod G., Ghetti B., Palacios J.M., Triarhou L.C.;  
 RT "Regional distribution of the alternatively spliced isoforms of beta  
 RT APP RNA transcript in the brain of normal, heterozygous and  
 RT homozygous weaver mutant mice as revealed by in situ hybridization  
 RT histochemistry.";  
 RL Brain Res. Mol. Brain Res. 17:340-346(1993).  
 RN [11]  
 RP INTERACTION WITH KNS2.  
 RX MEDLINE=21010507; PubMed=11144355;  
 RA Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;  
 RT "Axonal transport of amyloid precursor protein is mediated by direct  
 RT binding to the kinesin light chain subunit of kinesin-I.";  
 RL Neuron 28:449-459(2000).  
 RN [12]  
 RP C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;  
 RP THR-743; TYR-757; ASN-759 AND TYR-762.  
 RX MEDLINE=21408156; PubMed=11517249;  
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,  
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,  
 RA Kyriakis J.M., Nishimoto I.;  
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1

RT scaffolds Alzheimer's amyloid precursor protein with JNK.";  
 RL J. Neurosci. 21:6597-6607(2001).  
 RN [13]  
 RP INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.  
 RX MEDLINE=22028091; PubMed=11912189;  
 RA Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;  
 RT "Interaction of Alzheimer's beta-amyloid precursor family proteins  
 RT with scaffold proteins of the JNK signaling cascade.";  
 RL J. Biol. Chem. 277:20070-20078(2002).  
 RN [14]  
 RP INTERACTION OF CTF PEPTIDES WITH NUMB.  
 RX MEDLINE=22008109; PubMed=12011466;  
 RA Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,  
 RA Meucci O., McGlade J.C., Rakic P., D'Adamio L.;  
 RT "The gamma-secretase-generated intracellular domain of beta-amyloid  
 RT precursor protein binds Numb and inhibits Notch signaling.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).  
 RN [15]  
 RP GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.  
 RX MEDLINE=21437805; PubMed=11553691;  
 RA Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;  
 RT "The amyloid precursor protein (APP)-cytoplasmic fragment generated by  
 RT gamma-secretase is rapidly degraded but distributes partially in a  
 RT nuclear fraction of neurones in culture.";  
 RL J. Neurochem. 78:1168-1178(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions. Can promote transcription activation through binding  
 CC to APBB1/Tip60 and inhibit Notch signaling through interaction  
 CC with Numb. Couples to apoptosis-inducing pathways such as those  
 CC mediated by G(O) and JIP. Inhibits G(O) alpha ATPase activity (By  
 CC similarity). Acts as a kinesin I membrane receptor, mediating the  
 CC axonal transport of beta-secretase and presenilin 1. May be  
 CC involved in copper homeostasis/oxidative stress through copper ion  
 CC reduction. Can regulate neurite outgrowth through binding to  
 CC components of the extracellular matrix such as heparin and  
 CC collagen I and IV (By similarity). The splice isoforms that  
 CC contain the BPTI domain possess protease inhibitor activity (By  
 CC similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind  
 CC only weakly transient metals and have little reducing activity due  
 CC to substitutions of transient metal chelating residues. Beta-APP42  
 CC may activate mononuclear phagocytes in the brain and elicit  
 CC inflammatory responses. Promotes both tau aggregation and TPK II-  
 CC mediated phosphorylation (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis.  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits  
 CC its serine phosphorylation. Also interacts with GPCR-like protein  
 CC BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via





RP SEQUENCE OF 720-730, AND MASS SPECTROMETRY.  
 RX MEDLINE=21443797; PubMed=11483588;  
 RA Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;  
 RT "Distinct intramembrane cleavage of the beta-amyloid precursor protein  
 RT family resembling gamma-secretase-like cleavage of Notch.";  
 RL J. Biol. Chem. 276:35235-35238(2001).  
 RN [4]  
 RP ALTERNATIVE SPLICING.  
 RX MEDLINE=96187032; PubMed=8624099;  
 RA Sandbrink R., Masters C.L., Beyreuther K.;  
 RT "APP gene family. Alternative splicing generates functionally related  
 RT isoforms.";  
 RL Ann. N.Y. Acad. Sci. 777:281-287(1996).  
 RN [5]  
 RP TISSUE SPECIFICITY OF APPICAN.  
 RX MEDLINE=95263526; PubMed=7744833;  
 RA Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,  
 RA Mytilineou C., Margolis R.U., Robakis N.K.;  
 RT "The Alzheimer amyloid precursor proteoglycan (appican) is present in  
 RT brain and is produced by astrocytes but not by neurons in primary  
 RT neural cultures.";  
 RL J. Biol. Chem. 270:11839-11844(1995).  
 RN [6]  
 RP TISSUE SPECIFICITY OF ISOFORMS.  
 RX MEDLINE=97150061; PubMed=8996834;  
 RA Sandbrink R., Monning U., Masters C.L., Beyreuther K.;  
 RT "Expression of the APP gene family in brain cells, brain development  
 RT and aging.";  
 RL Gerontology 43:119-131(1997).  
 RN [7]  
 RP INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND  
 RP TYR-762.  
 RX MEDLINE=99127916; PubMed=9930726;  
 RA Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,  
 RA Suzuki T., Nairn A.C., Greengard P.;  
 RT "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the  
 RT Alzheimer's amyloid precursor protein.";  
 RL J. Neurochem. 72:549-556(1999).  
 RN [8]  
 RP INTERACTION WITH GNAO1, AND MUTAGENESIS OF 732-HIS-HIS-733.  
 RX MEDLINE=99162676; PubMed=10024358;  
 RA Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouilliot C.,  
 RA Valenza C., Prochiantz A., Allinquant B.;  
 RT "The amyloid precursor protein interacts with Go heterotrimeric  
 RT protein within a cell compartment specialized in signal  
 RT transduction.";  
 RL J. Neurosci. 19:1717-1727(1999).  
 RN [9]  
 RP CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.  
 RX MEDLINE=95256193; PubMed=7737970;  
 RA Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;  
 RT "The chondroitin sulfate attachment site of appican is formed by  
 RT splicing out exon 15 of the amyloid precursor gene.";  
 RL J. Biol. Chem. 270:10388-10391(1995).  
 RN [10]  
 RP BETA-AMYLOID METAL-BINDING.  
 RX MEDLINE=99316162; PubMed=10386999;

RA Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,  
 RA Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,  
 RA Bush A.I.;  
 RT "The A beta peptide of Alzheimer's disease directly produces hydrogen  
 RT peroxide through metal ion reduction.";  
 RL Biochemistry 38:7609-7616(1999).  
 RN [11]  
 RP BETA-AMYLOID ZINC BINDING.  
 RX MEDLINE=99343552; PubMed=10413512;  
 RA Liu S.T., Howlett G., Barrow C.J.;  
 RT "Histidine-13 is a crucial residue in the zinc ion-induced aggregation  
 RT of the A beta peptide of Alzheimer's disease.";  
 RL Biochemistry 38:9373-9378(1999).  
 RN [12]  
 RP IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF  
 RP GLY-704.  
 RX MEDLINE=21956095; PubMed=11959460;  
 RA Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;  
 RT "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-  
 RT peptide 1-42-associated oxidative stress and neurotoxicity.";  
 RL Biochim. Biophys. Acta 1586:190-198(2001).  
 RN [13]  
 RP PHOSPHORYLATION.  
 RX MEDLINE=97239592; PubMed=9085254;  
 RA Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,  
 RA Greengard P., Suzuki T.;  
 RT "The cytoplasmic domain of Alzheimer's amyloid precursor protein is  
 RT phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and  
 RT cultured cells.";  
 RL Mol. Med. 3:111-123(1997).  
 RN [14]  
 RP PHOSPHORYLATION ON SER-730.  
 RX MEDLINE=99262094; PubMed=10329382;  
 RA Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,  
 RA Greengard P., Nairn A.C., Suzuki T.;  
 RT "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid  
 RT precursor protein at Ser655 by a novel protein kinase.";  
 RL Biochem. Biophys. Res. Commun. 258:300-305(1999).  
 RN [15]  
 RP PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF  
 RP THR-743.  
 RX MEDLINE=99274744; PubMed=10341243;  
 RA Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,  
 RA Kirino Y., Greengard P., Suzuki T.;  
 RT "Role of phosphorylation of Alzheimer's amyloid precursor protein  
 RT during neuronal differentiation.";  
 RL J. Neurosci. 19:4421-4427(1999).  
 RN [16]  
 RP PHOSPHORYLATION ON THR-743.  
 RX MEDLINE=20396183; PubMed=10936190;  
 RA Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,  
 RA Greengard P., Kirino Y., Nairn A.C., Suzuki T.;  
 RT "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor  
 RT protein by cyclin-dependent kinase 5.";  
 RL J. Neurochem. 75:1085-1091(2000).  
 RN [17]  
 RP CARBOHYDRATE STRUCTURE OF APPICAN.

RX MEDLINE=21463085; PubMed=11479316;  
 RA Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,  
 RA Sugahara K., Robakis N.K.;  
 RT "Appican, the proteoglycan form of the amyloid precursor protein,  
 RT contains chondroitin sulfate E in the repeating disaccharide region  
 RT and 4-O-sulfated galactose in the linkage region.";  
 RL J. Biol. Chem. 276:37155-37160(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(O) and JIP. Inhibits  
 CC G(O) alpha ATPase activity. Acts as a kinesin I membrane receptor,  
 CC mediating the axonal transport of beta-secretase and presenilin 1  
 CC (By similarity). May be involved in copper homeostasis/oxidative  
 CC stress through copper ion reduction. Can regulate neurite  
 CC outgrowth through binding to components of the extracellular  
 CC matrix such as heparin and collagen I and IV (By similarity). The  
 CC splice isoforms that contain the BPTI domain possess protease  
 CC inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind  
 CC only weakly transient metals and have little reducing activity due  
 CC to substitutions of transient metal chelating residues. Beta-APP42  
 CC may activate mononuclear phagocytes in the brain and elicit  
 CC inflammatory responses. Promotes both tau aggregation and TPK II-  
 CC mediated phosphorylation (By similarity).  
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the  
 CC extracellular matrix and may regulate neurite outgrowth in the  
 CC brain.  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity). Interacts,  
 CC through a C-terminal domain, with GNAO1. Amyloid beta-42 binds  
 CC CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid  
 CC associates with HADH2 (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the

Query Match 91.2%; Score 198; DB 1; Length 770;  
 Best Local Similarity 92.9%; Pred. No. 3.1e-18;  
 Matches 39; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

Qy           1 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA 42  
             ||||| :|| |||||  
Db         672 DAEEFGHDSGFEVRHOKLVFFAEDVGSNKGAIIGLMVGGVVIA 713

DR PROSITE; PS00320; A4\_INTRA; 1.  
DR PROSITE; PS00280; BPTI\_KUNITZ\_1; FALSE\_NEG.  
DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
KW Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;  
KW Serine protease inhibitor.  
FT SIGNAL 1 18 POTENTIAL.  
FT CHAIN 19 780 ALZHEIMER'S DISEASE AMYLOID A4 PROTEIN  
FT HOMOLOG.  
FT CHAIN 682 724 BETA-AMYLOID PROTEIN (POTENTIAL).  
FT DOMAIN 19 711 EXTRACELLULAR (POTENTIAL).  
FT TRANSMEM 712 732 POTENTIAL.  
FT DOMAIN 733 780 CYTOPLASMIC (POTENTIAL).  
FT DOMAIN 323 382 BPTI/KUNITZ INHIBITOR.  
FT SITE 769 772 CLATHRIN-BINDING (BY SIMILARITY).  
FT DISULFID 327 378 BY SIMILARITY.  
FT DISULFID 336 361 BY SIMILARITY.  
FT CARBOHYD 560 560 N-LINKED (GLCNAC. . .) (POTENTIAL).  
SQ SEQUENCE 780 AA; 88238 MW; 60071BE94520191D CRC64;

Query Match 80.6%; Score 175; DB 1; Length 780;  
Best Local Similarity 83.3%; Pred. No. 3.3e-15;  
Matches 35; Conservative 2; Mismatches 5; Indels 0; Gaps 0;

Qy 1 DAEFRHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIA 42  
: | | : |||||  
Db 682 ETEDRQSTEEYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIA 723

#### RESULT 14.

A4\_FUGRU  
ID A4\_FUGRU STANDARD; PRT; 737 AA.  
AC O93279;  
DT 10-OCT-2003 (Rel. 42, Created)  
DT 10-OCT-2003 (Rel. 42, Last sequence update)  
DT 10-OCT-2003 (Rel. 42, Last annotation update)  
DE Alzheimer's disease amyloid A4 protein homolog precursor [Contains:  
DE Beta-amyloid protein (Beta-APP) (A-beta)].  
GN APP.  
OS Fugu rubripes (Japanese pufferfish) (Takifugu rubripes).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;  
OC Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;  
OC Tetraodontoidea; Tetraodontidae; Takifugu.  
OX NCBI\_TaxID=31033;  
RN [1]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=98252138; PubMed=9599080;  
RA Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;  
RT "Analysis of pufferfish homologues of the AT-rich human APP gene.";  
RL Gene 210:17-24(1998).  
CC -!- FUNCTION: Functional neuronal receptor which couples to  
CC intracellular signaling pathway through the GTP-binding protein  
CC G(0) (By similarity).  
CC -!- SUBCELLULAR LOCATION: Type I membrane protein.  
CC -!- SIMILARITY: Belongs to the APP family.  
CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
CC -----



DT 23-OCT-1986 (Rel. 02, Created)  
 DT 23-OCT-1986 (Rel. 02, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Tryptophan 2-monooxygenase (EC 1.13.12.3).  
 GN TMS1.  
 OS Agrobacterium tumefaciens (strain Ach5), and  
 OS Agrobacterium tumefaciens.  
 OG Plasmid pTiAch5, and Plasmid pTiA6NC.  
 OC Bacteria; Proteobacteria; Alphaproteobacteria; Rhizobiales;  
 OC Rhizobiaceae; Rhizobium/Agrobacterium group; Agrobacterium.  
 OX NCBI\_TaxID=176298, 358;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN=Ach5; PLASMID=pTiAch5;  
 RX MEDLINE=84207942; PubMed=6327292;  
 RA Gielen J., de Beuckeleer M., Seurinck J., Deboeck F., de Greve H.,  
 RA Lemmers M., van Montagu M., Schell J.;  
 RT "The complete nucleotide sequence of the TL-DNA of the Agrobacterium  
 RT tumefaciens plasmid pTiAch5.";  
 RL EMBO J. 3:835-846(1984).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RC PLASMID=pTiA6NC;  
 RX MEDLINE=84170374; PubMed=6584906;  
 RA Klee H., Montoya A., Horodyski F., Lichtenstein C., Garfinkel D.,  
 RA Fuller S., Flores C., Peschon J., Nester E., Gordon M.;  
 RT "Nucleotide sequence of the tms genes of the pTiA6NC octopine Ti  
 RT plasmid: two gene products involved in plant tumorigenesis.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 81:1728-1732(1984).  
 CC -!- CATALYTIC ACTIVITY: L-tryptophan + O(2) = indole-3-acetamide +  
 CC CO(2) + H(2)O.  
 CC -!- PATHWAY: Biosynthesis of auxins from tryptophan; first step.  
 CC -!- MISCELLANEOUS: THE SEQUENCE SHOWN IS THAT OF ACH5.  
 CC -!- SIMILARITY: SIGNIFICANT HOMOLOGY TO THE ADENINE BINDING REGION OF  
 CC P-HYDROXYBENZOATE HYDROXYLASE FROM P. FLUORESCENS. IT SEEMS THAT  
 CC THIS PROTEIN BINDS ADENINE EITHER AS SUBSTRATE OR COFACTOR.  
 CC -----  
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 CC -----  
 DR EMBL; K02554; AAA92550.1; -.  
 DR PIR; A04497; QQAG4T.  
 DR InterPro; IPR000759; Adrndx\_reductase.  
 DR InterPro; IPR002937; Amino\_oxidase.  
 DR InterPro; IPR006064; Glycosidase.  
 DR InterPro; IPR000205; NAD\_BS.  
 DR Pfam; PF01593; Amino\_oxidase; 1.  
 DR Pfam; PF02027; RolB\_RolC; 1.  
 DR PRINTS; PR00419; ADXRDTASE.  
 KW Oxidoreductase; Monooxygenase; Auxin biosynthesis; Crown gall tumor;  
 KW Plasmid.  
 FT VARIANT 718 719 NR -> IQ (IN PTIA6NC).



FT VARIANT 721 721 P -> A (IN PTIA6NC).  
SQ SEQUENCE 755 AA; 83947 MW; 9FD2B83FEA001A4D CRC64;

Query Match 28.6%; Score 62; DB 1; Length 755;  
Best Local Similarity 41.7%; Pred. No. 2.2;  
Matches 15; Conservative 6; Mismatches 9; Indels 6; Gaps 1;

Qy 7 DSGYEVHHQKLVEFFAEDVGSNKGAIIGLMVGGVVIA 42  
||| :: || || | |:| : |:|  
Db 223 DSG-----RIGFFPEDVPKPKVAVIGAGISGLVVA 252

Search completed: July 15, 2004, 18:04:17  
Job time : 15 secs